

*February 2013*

## NIEHS Spotlight



### [NIEHS welcomes NINDS director](#)

National Institute of Neurological Disorders and Stroke Director Story Landis, Ph.D., explored the topic “Managing in Difficult Times” in a talk at NIEHS Jan. 17.



### [NIDDK director keynotes MLK observance](#)

NIEHS observed the birthday of Martin Luther King Jr. Jan. 25 with a presentation on obesity, kidney, and metabolic disease research by Griffin Rodgers, M.D.



### [Tickner encourages alternative solutions in green chemistry talk](#)

According to University of Massachusetts Lowell researcher Joel Tickner, Sc.D., the time has come for scientists to take a more solutions-driven approach.



### [Oil spill researchers tell what they learned](#)

More than 1,000 scientists gathered in New Orleans Jan. 21-23 to discuss the 2010 Deepwater Horizon oil spill and its effects on the environment and communities.



### [Laber named head of Comparative Medicine Branch](#)

NIEHS Scientific Director Darryl Zeldin, M.D., announced Jan. 22 that Kathy Laber, D.V.M., will join NIEHS in June as chief of the Comparative Medicine Branch.

## Science Notebook



### [Autoimmunity expert delivers distinguished lecture](#)

Noel Rose, M.D., Ph.D., a leading autoimmunity expert, came to NIEHS Jan. 8 and presented “Myocarditis: an environmentally induced autoimmune disease.”



### [Nano meeting tackles consumer exposures](#)

An impressive lineup of speakers at the NIEHS Nano Exposure Workshop Jan. 9-10 underscored how much scientists still don't understand about health effects.



### [NIEHS researcher assists in study of Norwegian women](#)

The study suggests that expectant mothers who forgo influenza vaccination may face increased risk of fetal loss if they become ill with the virus.



### [Exploring the haunting legacy – benomyl and Parkinson's](#)

NIEHS-funded research reports on a newly discovered mechanism in Parkinson's disease, a finding that could point to an innovative therapeutic approach.



### [PEPH launches new podcast series](#)

Researchers working in partnership with community groups are featured in a new podcast series by the NIEHS Partnerships for Environmental Public Health program.

## NIEHS Spotlight



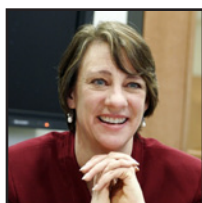
### [Lancet commentary targets non-communicable diseases](#)

NIEHS scientists and an international group of collaborators published a commentary in the journal's Jan. 5 issue about early-life prevention of non-communicable diseases.



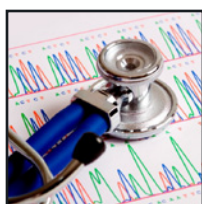
### [NIEHS answers the call in the aftermath of Sandy](#)

A special Federal Emergency Management Agency allocation approved Dec. 29 is helping NIEHS expand safety training in the aftermath of Hurricane Sandy.



### [Hrynkow named to head network of viral specialists](#)

Former NIEHS Associate Director Sharon Hrynkow, Ph.D., was appointed in December 2012 as president of the nonprofit Global Virus Network of Baltimore.



### [NIEHS opens search for clinical director](#)

In January, NIEHS launched a search for a director of the clinical research program at the senior investigator, tenure-eligible level, with a closing date of Feb. 28.



### [Research fellow begins career in medical writing](#)

NIEHS research fellow Jeffrey Stumpf, Ph.D. began his new position Jan. 2 as a medical writer with MedThink SciCom in Raleigh, N.C.



### [Grantees elected fellows of AAAS](#)

Five NIEHS grantees will be among new fellows honored this year by the American Association for the Advancement of Science.

## Science Notebook



### [Air pollution pinpointed as major global health problem](#)

Findings from the Global Burden of Disease Study 2010 underscore the conventional wisdom that air pollution is a major health risk factor across the globe.



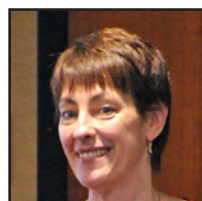
### [Ho group uses saliva for study on methylation in asthma](#)

Using saliva samples, a new study led by NIEHS grantee Shuk-mei Ho, Ph.D., has identified epigenetic changes to a new biomarker associated with asthma.



### [Prenatal inflammation linked to autism risk](#)

A team of U.S. and Finnish researchers found that elevated C-reactive protein, a marker of systemic inflammation, was tied to increased autism risk.



### [Uncovering the genetic component in nicotine addiction](#)

Psychiatrist Laura Bierut, M.D., explored the interplay of environment and genes in smoking behaviors during a talk at NIEHS Jan. 23.



### [NIEHS research featured in The Journal of Immunology](#)

The new findings expand scientists' understanding of an important receptor and may lead to discovery of a therapeutic target for viral-induced chronic inflammatory illnesses.

## NIEHS Spotlight



### [Outreach educator honored with SOT Public Communications Award](#)

The group recognized Marti Lindsey, Ph.D., for efforts to develop and disseminate environmental health materials related to issues of concern in the southwestern U.S.



National Institutes  
of Health

### [New logo emphasizes NIH identity](#)

The logo was developed over the past year as part of a larger effort to strengthen the impact of NIH communications.

## Inside the Institute



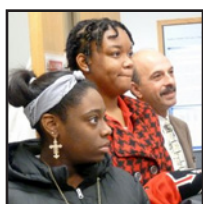
### [NIEHS surpasses 2012 CFC goal](#)

It was another record setting year for the NIEHS participation in the Combined Federal Campaign, with pledges exceeding the 2012 goal of \$115,000.



### [NIEHS biologist honored for award-winning photography](#)

A thriving amateur photographer, NIEHS biologist John Petranka is being honored by Wildlife in North Carolina magazine for three of his wildlife photos.



### [Neighbors in the house](#)

A visiting high school group's science teacher, Andrew Joseph, Ph.D., was a postdoctoral fellow at NIEHS during the mid-1980s.

## Science Notebook



### [This month in EPH](#)



News features in the February issue of Environmental Health Perspectives describe potentially promising developments in environmental health.

## Extramural Research

### [Extramural papers of the month](#)

- [Black carbon from kerosene lamps contributes to climate change](#)
- [Bioanalytical tool measures toxicity of bioavailable complex mixtures](#)
- [Developing new chemicals free of endocrine disruptors](#)
- [Mechanism for increased Parkinson's disease risk from benomyl exposure](#)

## Intramural Research

### [Intramural papers of the month](#)

- [Interdependence of estrogen receptor alpha domains in maintaining male fertility](#)
- [Mismatch repair balances leading and lagging strand DNA replication fidelity](#)
- [Novel role of Galpha\(i\) subfamily of G-proteins in axial skeleton development](#)
- [The involvement of leptin in fatty liver disease](#)

## Calendar of Upcoming Events

- **Feb. 5**, in Rodbell Auditorium, 11:00 a.m.-12:00 p.m. — Superfund Research Program Wetterhahn Award Seminar with 2012 winner Monica Ramirez-Andreotta.
- **Feb. 6**, in Rodbell Auditorium, 8:30 a.m.-4:30 p.m. — Rx for Science Literacy Workshop
- **Feb. 8**, in Keystone 1003AB, 10:00-11:00 a.m. — Office of the Director seminar with Doug Stevens, Ph.D., describing “SKC [Salish Kootenai College] Life Sciences Program: Engaging Native American Studies in STEM through a Research-Intensive Curriculum”
- **Feb. 8 offsite event**, in Levine Science Research Center, Room A247, at Duke University, 12:00-1:30 p.m. — Integrated Toxicology and Environmental Health Seminar Series, featuring Michael Ashner, Ph.D., discussing “From *C. elegans* to humans: understanding Mn-induced neurodegeneration”
- **Feb. 13**, in Rodbell Auditorium, 1:00-2:00 p.m. — NIEHS Annual Awards Ceremony
- **Feb. 19**, in Keystone 1003AB, 10:00-11:00 a.m. — Keystone Science Seminar Series featuring Andrew Feinberg, M.D., The Molecular Basis of Common Human Disease
- **Feb. 20-21**, in Rodbell Auditorium, 8:30 a.m.-5:00 p.m. — National Advisory Environmental Health Sciences Council
- **March 1 offsite event**, at Duke University’s Doris Duke Center, 8:30 a.m.-3:00 p.m. — Integrated Toxicology and Environmental Health Program [Spring Symposium](#), “How Epigenomic Effects Mediate Persisting Actions of Developmental Toxicants”
- View More Events: [NIEHS Public Calendar](#)



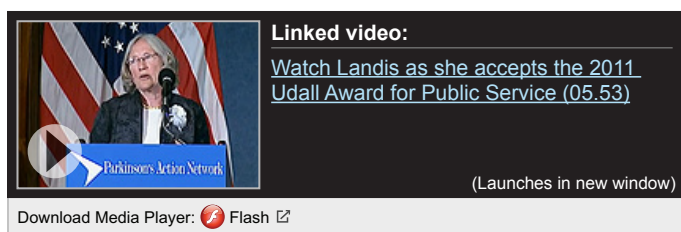
# NIEHS Spotlight

## NIEHS welcomes NINDS director

By Eddy Ball

National Institute of Neurological Disorders and Stroke (NINDS) Director [Story Landis, Ph.D.](#), was at NIEHS Jan. 17 to give a talk on “Managing in Difficult Times: The NINDS Experience.”

Her topic wasn’t the fascinating science supported by her institute, but instead the difficult decisions NIH leaders need to make about programs, to deal with flat budgets and possible spending cuts on the horizon. As NIEHS/NTP Director Linda Birnbaum, Ph.D., said in her introduction of Landis, “She’s going to be talking about reality.”



*Landis said she is dedicated to making sure NINDS can support the best science and as much of it as possible. Landis made it clear that she refuses to let loyalty to underperforming programs keep NINDS from looking ahead to such needs as driving drug development, discovering ways to prevent such diseases as epilepsy, and devoting more resources to traumatic brain disorder research. (Photo courtesy of Steve McCaw)*

### (Re)visioning research programs and priorities

Landis became the head of NINDS in 2003, during the final year of what NIH veterans remember fondly as the [doubling](#) — a five-year period during which the total budget for biomedical research at NIH grew to twice its fiscal year 1998 level. Almost before she was settled in her new office, Landis began to face difficult budget and program choices, when the heady times of unprecedented growth and funding for new initiatives gave way to what she described as the undoubling, as revenue in real dollars stabilized, while inflation pushed expenses ever higher.

According to Landis, the NINDS funding challenge is complicated by the other challenges her institute faces. These include the sheer number of neurological diseases NINDS scientists study, many of them quite rare, and little or no interest on the part of drug companies, or pharma, to devote resources to ushering promising discoveries through the long and expensive process of clinical trials. Pharma, she explained, has been discouraged by failed trials, a glut of drugs already on the market, and the small markets for new drugs.



*After talking about Landis’ stellar scientific career, Birnbaum set the stage for a narrative of struggle with financial and programmatic challenges at NINDS. Birnbaum has warned grantees and employees, on several occasions, of budget-driven change that may very well be on the horizon. (Photo courtesy of Steve McCaw)*

What NINDS needed — and what other NIH institutes may soon face, as well — was a radical restructuring of priorities and programs. So Landis and her leadership began the often painful process of creating innovative translational programs, and redirecting resources from traditional funding designs to new ones.

Along the way, that meant taking what were sometimes extreme measures. These included sacrificing sacred cows, such as underperforming Morris K. Udall Centers of Excellence for Parkinson's Disease Research; initiating more extensive and more frequent review of programs; asking tougher questions of researchers and pushing for transparency, as well as the reporting of negative results; pursuing new ways of conducting public-private partnerships to give pharma more incentive to pursue new drug development; introducing NeuroNEXT, which features a central institutional review board that reduced protocol to patient time from two years to two months; and institutionalizing sunset provisions for programs.

Unlike past practices, when project grants now end, Landis explained, "You have to do something entirely different."

### Feeling the pain

Under Landis' direction, every part of NINDS, from its relatively small in-house research group to its extensive grants portfolio, felt the pressure to become leaner and meaner, by cutting underperforming programs and streamlining operations to cut administrative overhead.

The audience, who ranged from lead researchers from the in-house laboratory groups at NIEHS and grants portfolio analysts and administrators, to members of the NIEHS Office of Management's Financial Management Branch, naturally had questions about the push back Landis and her team faced from interest groups. She answered their questions candidly and concluded with her bottom line.

"We are just really tough," she said.



*There was no shortage of questions following the presentation. NIEHS Deputy Director Rick Woychik, Ph.D., left, joined DERT Program Analyst Jerry Phelps, center, and Health Science Administrator Kimberly McAllister, Ph.D., as they waited their turns to query Landis. (Photo courtesy of Steve McCaw)*



*NIEHS lead researcher John Cidlowski, Ph.D., was one of several intramural scientists on hand for the talk. One effect of Landis' realignment of resources at NINDS was cutting the number of lead researchers there by some 33 percent. (Photo courtesy of Steve McCaw)*



*NIEHS Division of Extramural Research and Training (DERT) Deputy Director Pat Mastin, Ph.D., right, and Grants Management Specialist Molly Puente, Ph.D., were among many in the audience who were keenly interested in how Landis redirected grant resources at NINDS. (Photo courtesy of Steve McCaw)*


[Return to Table of Contents](#)



# NIDDK director keynotes MLK observance

By Eddy Ball

NIEHS observed the birthday of Martin Luther King Jr. Jan. 25 with a presentation on obesity, kidney, and metabolic disease research by [Griffin Rodgers, M.D.](#), director of the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). Rodgers' talk was sponsored by the NIEHS Office of the Director, Raleigh Durham Area Chapter of Blacks In Government (BIG), and NIEHS Diversity Council.





**What are the diabetes ABCs?**

**Linked video:**

[Watch a short video featuring Rodgers' recommendations for people with diabetes \(05:29\)](#)

(Launches in new window)

Download Media Player:  Flash 

In her introduction of Rodgers, NIEHS/NTP Director Linda Birnbaum, Ph.D., described the close partnership the two institutes continue to enjoy, with their common interest in equality, primary prevention, and the environment. “We share a lot of interest in environmental exposures and the increase in obesity and type 2 diabetes,” she said.

At several points in his talk, Rodgers also reinforced the ways the missions of NIEHS and NIDDK dovetail, underscoring his institute’s growing awareness of the role of gene-environment interactions in health and disease. “I feel a real kinship, because the missions of NIDDK and NIEHS are really one in the same – preventing illness, improving people’s well-being, and saving lives. And, much of the work that we [NIDDK] are trying to achieve ties very closely into the work being done here at NIEHS.”

Rodgers connected his institute’s research mission to the larger social issues of equality in terms of health disparities and environmental justice, invoking King’s spirit in the quest to prevent and better treat a range of diseases that disproportionately affect people of color. “One of our society’s greatest injustices is the fact that African-Americans, Latinos, and other people of color are more likely to get sick and die younger than the population as a whole — and, not coincidentally, [because of] the fact that members of these racial and ethnic groups are more likely to be exposed to toxic environments, because of the neighborhoods where they live.”



*Birnbaum listed a few of Rodgers’ many accomplishments during his 11 years as director and deputy director of NIDDK. “I just have to say, that was great,” she exclaimed at the end of his talk. “You just have to come back, so that more people can have the opportunity to talk with you one-on-one.” (Photo courtesy of Steve McCaw)*



*“There’s a direct correlation between the mission areas of NIDDK and NIEHS and those diseases that disproportionately affect people of color. This is really the mission that moves me at a scientific level, but also at a moral level,” Rodgers told the audience. “Serving others is the ultimate mission of NIDDK and it certainly is the ultimate mission of NIEHS — a mission of science and medicine at its very best.” (Photo courtesy of Steve McCaw)*

## Obesity fuels multiple medical problems

Like several other conditions, obesity and the diseases it fuels are chronic, common, costly, and consequential. These diseases, which range from diabetes and cardiovascular disease to end-stage renal disease and several types of cancer, have increased in terms of incidence and financial burden over the past few decades. According to Rodgers, this trend suggests that, along with genetic predisposition, environmental triggers, including diet, lifestyle, and other environmental exposures, may play an important role. African-Americans, Native Americans, Latinos, and other people of color experience rates of some of these diseases that are two to four times those of whites.

In the past twenty years alone, Rodgers said, obesity rates in the U.S. have tripled, growing from 10 percent or less in 1990 to more than 30 percent in 2010. Annual costs for treating obesity and related diseases range from conservative estimates of \$27 billion for chronic kidney diseases to \$174 billion for type 2 diabetes. Increasingly, younger people are developing these diseases, with as many as 17 percent of children now considered obese, and children in their early teens developing what used to be considered adult-onset type 2 diabetes.

NIDDK has supported a number of clinical trials to compare intervention outcomes and cost effectiveness in reducing the risk of diabetes progression, and it has translated findings into alternative ways of preventing and treating disease. After findings emerged, indicating that lifestyle changes in diet and exercise, combined with counseling, were more effective than medication, NIDDK funded an experiment, involving a group counseling and exercise program at YMCAs, as a model for what might become a community-based, cost-effective national network to help combat diabetes and prediabetes.

As Rodgers returned to King at the end of his presentation, he quoted from what is known as the civil rights leader's drum major sermon. "Life's most persistent and urgent question is, what are you doing for others?" King had challenged his audience, observing that everyone, no matter how few his or her gifts and talents, can reach out to achieve greatness by serving others. "Let us seek to be the best servants."

For more information, visit the NIDDK website at <http://www2.niddk.nih.gov>.

## Translating research into education and outreach

Like NIEHS, with its Partnerships for Environmental Public Health, Superfund Research, and Workers' Education and Training programs, NIDDK also translates research into educational and public awareness materials, which it posts prominently on its [home page](#). Materials are reader friendly and available in as many as 20 different languages, with messages geared to patients, families, healthcare providers, and even school personnel who need to accommodate children with handicaps related to their conditions.

"One group that we're extremely interested in getting this message to are women who have had a history of gestational diabetes," Rodgers said. Some 5 to 7 percent of pregnancies experience this type of diabetes, with long-term risk among the mothers and their newborn children for developing diabetes.

"This material is not only scientifically valid," Rodgers said of NIDDK educational publications, "but [also] has been socially marketed to be sure that the message we're trying to get out is socially and contextually appropriate."

Rodgers also communicates by radio throughout the nation, with regular "Healthy Moments" segments. He said that one of NIDDK's greatest challenges is overcoming the widespread fatalistic assumption that obesity-related diseases are inevitable. Today, more people than just a few years ago consider diabetes to be an important health problem that should be addressed as early as possible. Still, nearly two-thirds of those polled still don't recognize its significance or understand how great a role diet and lifestyle, throughout an individual's lifespan, play in the development and progression of disease.





*BIG leaders Veronica Robinson, left, and Annette Rice both applauded Rodgers' work to address health disparities. "Because of the weather, he's going to fly out early, but we will have him back, hopefully later this year," Robinson told the audience following Rodgers' presentation. (Photo courtesy of Steve McCaw)*



*Rodgers drew an audience that included representatives from groups throughout the Institute, including Deputy Associate Director of Management Chris Long, right, and NTP pathologist Robert Sills, D.V.M., Ph.D. (Photo courtesy of Steve McCaw)*



*NIEHS Deputy Scientific Director William Schrader, Ph.D., was among the audience members who took advantage of the unusually generous 20 minutes set aside for questions and answers. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# Tickner encourages alternative solutions in green chemistry talk

By Ian Thomas

Many toxicology studies operate with the goal of identifying which chemicals are harmful to the public, then exploring the various mechanisms that make them so. However, according to [Joel Tickner, Sc.D.](#), an associate professor at the University of Massachusetts Lowell, the time has come for scientists to take a more solutions-driven approach.

“The role of basic toxicology will always be to understand what chemicals make people sick, and why,” said Tickner, an environmental health researcher. “There comes a point, however, when scientists must stop reacting to problems and start looking for new alternatives to solve them.”

This notion of alternatives-based research is the foundation for a field Tickner and others refer to as alternatives assessment.

## A focus on functionality

As Tickner explained, while manufacturers and consumers alike are always interested to know which products may be harmful to their health, often times they’re more interested in knowing which ones aren’t.

“In the end, it’s all about functionality,” said Tickner. “If company X discovers that bisphenol A could be harmful to its customers, odds are it’ll be less interested in understanding the science behind why that is, and more interested in finding chemical alternatives that are both safe and equally as efficient with regard to product application.”

NIEHS Toxicology Liaison and lecture host [Chris Weis, Ph.D.](#), agrees.

## Eight steps of alternatives assessment

- Engage stakeholders
- Define the goal
- Identify chemicals of high concern
- Prioritize uses for further evaluation
- Identify and prioritize alternatives
- Compare alternatives
- Select an alternative
- Promote the adoption of safer alternatives



*Tickner noted that alternatives assessment is a critical approach to ensuring informed substitution, so that actions to remove a chemical of concern do not lead to new problems. (Photo courtesy Steve McCaw)*



*Weis represented the NIEHS Office of the Director, which sponsored Tickner’s presentation. (Photo courtesy of Steve McCaw)*



“Chemical engineers are beginning to think of toxicity as a design flaw in their products, and they need reliable tools to screen for safer alternatives,” said Weis, who gave the talk’s introductory remarks. “In many ways, this requires scientists to be more proactive in how they examine these issues, and NIEHS is proud to be a part of that developmental process.”

### **An institutional investment**

According to Tickner, many companies such as Nike and Walmart have already made substantial investments in alternatives assessment, as have a number of federal agencies.

“Collaboration is the key,” he stated. “We’ve set up an array of networks, both in and out of government, to help researchers share information, and it’s our hope that investments like these will lead to new innovations that benefit everyone.”

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)

[Return to Table of Contents](#)

## **Oil spill researchers tell what they learned**

*By Christine Flowers*

More than 1,000 scientists gathered in New Orleans Jan. 21-23 to share what they’ve learned so far about the 2010 Deepwater Horizon oil spill and its effects on the environment and communities. The [Gulf of Mexico Oil Spill and Ecosystem Science Conference](#) was sponsored by the BP’s Gulf of Mexico Research Initiative (GoMRI), along with 13 other organizations, including NIEHS. The event was the first public presentation of research findings and an opportunity for government agencies, academia, and private industry to build partnerships focused on sustaining long-term environmental health.

“It was important for NIEHS to be part of this conference, because research on human health needs to be included in the broad discussion of ecosystem restoration,” said Senior Advisor Allen Dearry, Ph.D., who represented NIEHS on the conference steering committee and served as co-chair for the conference sessions on public health impacts of the oil spill.

In total, NIEHS staff and grantees gave 12 presentations and 10 poster sessions on NIEHS-supported recovery efforts, including the [GuLF STUDY](#), the university-community research projects funded by \$25 million in [NIH grants](#), the toxicology testing of oil and dispersants, and safety training for cleanup workers.



*Allen was selected by President Obama to lead the federal response to the Deepwater Horizon oil spill as the National Incident Commander. (Photo courtesy of the U.S. Naval Academy)*



## Prevailing themes

Over the course of the three-day symposium, some common themes prevailed. First, there was broad consensus that emergency response plans should allow research efforts to begin on day one of a disaster. Second, researchers should collect as much data about the people as they do about the biophysical environment. And third, response and research must address the human dimension, including health, economic, and social stressors.

Retired U.S. Coast Guard Adm. Thad Allen, who headed the oil spill Unified Command, gave the opening keynote speech for the conference. “One of the final actions I took was to order the collecting of water samples and oil samples for research ... We probably gave up our chance to get baselines,” Allen said. “We need to come up with a science response plan, to go along with the disaster response plan. I would endorse creating a science team with the necessary background and security credentials already in place.”

Maureen Lichtveld, M.D., an NIEHS grantee and chair of the Tulane University Department of Global Environmental Health Sciences, expanded this idea in her plenary talk, saying, “We need upfront approval to do human subjects research — a shovel ready approval — and a plan on the shelf.”

A shortage of baseline data posed a serious challenge for all the scientists who presented their research, whether they were studying people, sea life, plants, or water quality. “We need to know the state of the environment, so we can measure change,” said John Farrington, Ph.D., scientist emeritus at Woods Hole Oceanographic Institution. “We know that oil spills are one of the multiple stressors on the Gulf of Mexico ecosystems. The next generation of scientists needs to make sure we are better prepared with updated baselines.”

## The ecosystem includes people too

“The health of the environment and the health of the community are inextricably linked,” Lichtveld said. “Let’s break down the silos of doing ecosystem research separate from health research.”

Michael Orbach, Ph.D., director of the Coastal Environmental Management Program at Duke University, said there is a lack of social science in environmental policy. “We know a lot more about the fish than we know about the fisherman,” he said, as he called for more research on socioeconomic impacts. Orbach made the point that economic stress influences social behavior and resiliency — a word heard often during the

## Conference Sponsors

- Gulf of Mexico Research Initiative (GoMRI)
- American Petroleum Institute (API)
- Bureau of Ocean Energy Management (BOEM)
- Consortium for Ocean Leadership
- Gulf of Mexico Alliance
- Gulf of Mexico University Research Collaborative (GOMURC)
- National Aeronautics and Space Administration (NASA)
- National Institute of Environmental Health Sciences (NIEHS)
- National Oceanic and Atmospheric Administration (NOAA)
- National Science Foundation (NSF)
- U.S. Geological Survey (USGS)
- U.S. Food and Drug Administration (FDA)
- Subcommittee on Ocean Science and Technology (SOST)
- Sea Grant (Texas, Louisiana, Florida, Mississippi, Alabama)



*Lichtveld told conference attendees that NIEHS was active in the oil spill recovery and was funding many health studies in partnership with Gulf coast communities and universities. (Photo courtesy of Tulane University)*

conference, meaning the ability for ecosystems and communities to bounce back after a disaster. “As scientists, we need to document the benefits, as well as the costs, of the oil industry. There is a balance that is not always acknowledged by my friends, the marine biologists.”

### Local partners

During the conference, NIEHS/NTP Director Linda Birnbaum, Ph.D., and NIEHS Senior Medical Advisor Aubrey Miller, M.D., set aside an evening to meet with state health officials from Louisiana, Alabama, Mississippi, and Florida. NIEHS program staff joined in to answer questions and provide research updates.

“We want to thank you for everything that you’ve done to support NIEHS studies in your communities,” said Birnbaum. “We simply could not do the research without you.”



*Public Health Session co-chairs Dearry, left, and University of Alabama at Birmingham researcher Julia Gohlke, Ph.D., joined NIEHS epidemiologist Richard Kwok, Ph.D., center, who presented an overview of the NIEHS Gulf STUDY, a health study for oil spill clean-up workers. (Photo by Christine Flowers)*



*National Toxicology Program toxicologist Cynthia Rider, Ph.D., left, gave a presentation on NTP’s polycyclic aromatic hydrocarbon research. NTP’s Scott Masten, Ph.D., was on hand to answer questions. (Photo by Christine Flowers)*

[Return to Table of Contents](#)

## Laber named head of Comparative Medicine Branch

NIEHS Scientific Director Darryl Zeldin, M.D., announced Jan. 22 that Kathy Laber, D.V.M., will join NIEHS in June as chief of the Comparative Medicine Branch (CMB), attending veterinarian, and animal program director.

Currently, Laber is a professor in the Department of Comparative Medicine at the Medical University of South Carolina (MUSC) and director of the Laboratory of Animal Resources for the Ralph H. Johnson VA Medical Center.

Laber received her D.V.M. in 1984 from Michigan State University and completed her residency in Laboratory Animal Medicine at Bowman Gray School of Medicine. She also completed a master’s in molecular and cellular pathobiology at Wake Forest University in 1988.

Throughout her career, Laber has been active in many national and international organizations within her field. She is the immediate past president of the American Association for Laboratory Animal Science, an educational organization that serves a membership of 13,000 professionals dedicated to supporting quality animal research.

Laber served as president of the Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC). In her 16 years with AAALAC she conducted more than 170 site visits in the U.S. and abroad. She has also served on the American College of Laboratory Animal Medicine and the Association of VA Veterinary Medical Officers. Additionally, she was a primary reviewer for the multimillion dollar National Defense sponsored project, “Study of Potential Benefits of Assistive Dogs for Veterans with Mental Health Diagnoses,” and she is now serving on the Safety and Data Monitoring Board for the project.



*Newly appointed CMB Chief Laber (Photo courtesy of MUSC)*

[Return to Table of Contents](#)

## Lancet commentary targets non-communicable diseases

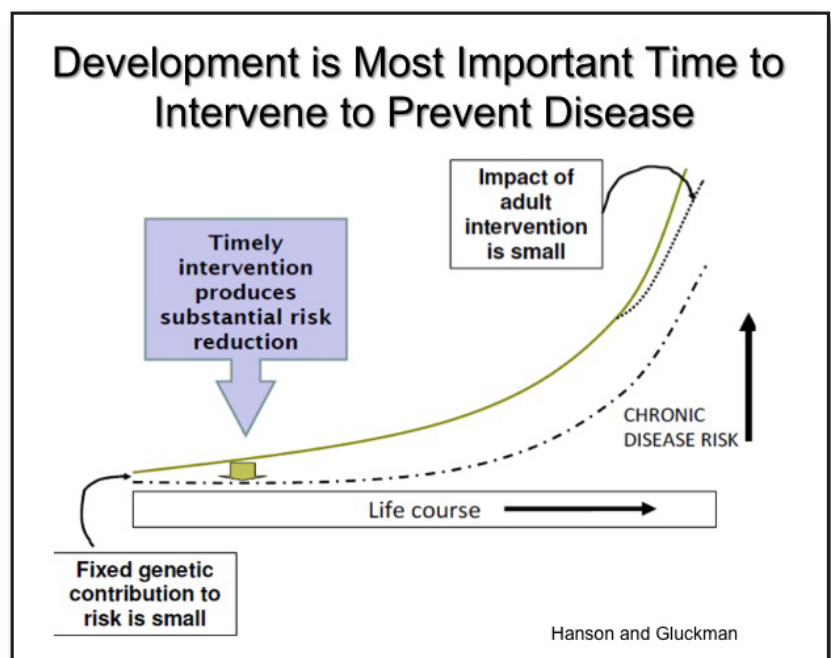
*By Eddy Ball*

NIEHS scientists and an international group of collaborators published a [commentary](#) about early-life prevention of non-communicable diseases (NCDs), in the Jan. 5 issue of the journal *The Lancet*. The findings are the outcome of a session held May 13, 2012, prior to the third annual international conference on Prenatal Programming and Toxicity (PPTOX III) in Paris ([see story](#)).

In their comment, lead author NIEHS Senior Advisor for Public Health [John Balbus, M.D.](#), and colleagues argue that much more attention is needed on early-life interventions, such as alleviation of poverty, optimization of nutrition, and reduction of toxic exposures, to curtail the increasing prevalence of NCDs, including diabetes, cardiovascular disease, and cancer.

### NCDs in developing countries

“NCDs underlie almost two-thirds of all global deaths,” the authors wrote. NCDs have a disproportionate impact on the poorest and most vulnerable populations in low-income and middle-income countries, with the greatest exposure to such environmental contaminants as metals, pesticides, persistent organic pollutants, and chemicals.



*This slide from Heindel's presentation in Paris emphasized that exposure prevention in early life can have a substantial impact on epigenetic alterations during fetal and childhood development that influence the risk of chronic disease later in life. (Graphic courtesy of Jerry Heindel)*



“Substantial reductions of NCD risks could be achieved through the use of existing maternal-child health platforms, to educate mothers about both nutritional and environmental exposures, and to integrate the health promotion and disease prevention agendas within social and economic development efforts,” they argue.

According to the authors, many NCDs that develop in adulthood are rooted in epigenetic alterations caused by *in utero* and early childhood experiences, pointing to a window of susceptibility during development where interventions may have the greatest effect. “Early life interventions,” they maintain, “can [also] reduce the perception of blame that the individual’s own lifestyle has caused his or her disease.”

In addition to Balbus, NIEHS contributors included NIEHS/NTP Director Linda Birnbaum, Ph.D., Health Scientist Administrator Jerry Heindel, Ph.D., and grantee Philippe Grandjean, M.D.

*Citation:* Balbus JM, Barouki R, Birnbaum LS, Etzel RA, Gluckman PD, Grandjean P, Hancock C, Hanson MA, Heindel JJ, Hoffman K, Jensen GK, Keeling A, Neira M, Rabadán-Diehl C, Ralston J, Tang KC. 2013. Early-life prevention of non-communicable diseases. *Lancet* 381(9860):3-4.

[Return to Table of Contents](#)

## NIEHS answers the call in the aftermath of Sandy

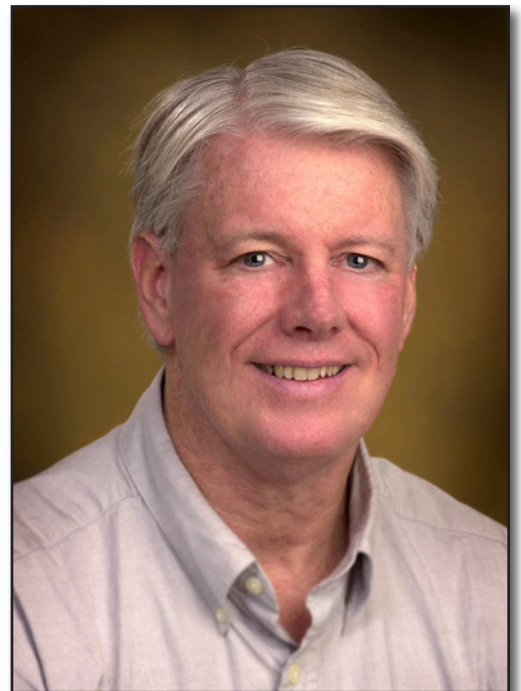
*By Eddy Ball*

A special Federal Emergency Management Agency (FEMA) allocation Dec. 29, 2012, is helping NIEHS expand safety training in the aftermath of Hurricane Sandy. The FEMA mission assignment that kicked off Jan. 8 with a session hosted by the New York City Housing Authority will support additional training for several thousand more people.

“It’s been both about creating public awareness of health and safety issues, as well as specific, more advanced training for people who are responders,” said WETP Director Chip Hughes. “Up to this point, it’s been mostly geared for volunteers and day laborers, tailored to what jobs people have been doing and what prior training, if any, they have about environmental health issues.”

“We have a team that’s evaluating OSHA [Occupational Safety and Health Administration] personal sampling data from people involved in the response,” Hughes explained. “We’re using it for our own purposes to evaluate what are the important exposures patterns.”

Hughes said the NIEHS involvement would probably last for at least a year, as it did in previous natural disasters, such as Katrina. He said he hopes for additional funding to support training on effective remediation of mold and other storm-related damage that affect the health of workers and residents. Hughes and his staff have rotated their onsite visits to New York and New Jersey over the past three months.



*“It’s still staggering to see what’s happened,” Hughes said of his last visit to the area.  
“I think mold is going to be a huge problem.”  
(Photo courtesy of Steve McCaw)*

## Taking advantage of a worker training infrastructure

The NIEHS Worker Education and Training Program (WETP) grantees have supplied worker safety awareness training, through existing programs in their New York and New Jersey communities, since the disaster hit Oct. 29, 2012. Members of the New York-New Jersey Consortium worked with representatives of the U.S. Environmental Protection Agency (EPA), OSHA, and state agencies to support responders, who range from well-trained public safety employees to municipal workers, volunteers, and subcontractors with little or no formal training.

In both New York and New Jersey, WETP supports a vigorous network of safety and health training organizations. This includes union-based programs, university and community college programs, and community nonprofits. It also includes the nonprofit training branch of the N.J. Highway Patrol. In total, over the past five years, these organizations have provided more than 9,000 courses for some 155,000 workers on a wide variety of safety and health topics. The primary focus has been hazardous waste operations and emergency response (hazwoper), with nearly 14,000 workers in New York and New Jersey alone having received training. The awardees have the capacity to provide training on disaster response, incident command systems, lead, asbestos, mold remediation, confined space, and numerous other topics, including what is known as lockout/tagout to prevent injury by disabling hazardous energy sources, such as electrical, pneumatic, and chemical equipment exposed or damaged during a disaster.

The awardees include the New York-New Jersey Consortium, which includes the University of Medicine and Dentistry of New Jersey; Hunter School of Health Sciences; New York Committee for Occupational Safety and Health; New Jersey State Police; University at Buffalo; New York City District Council of Carpenters Labor Technical College; and the Universidad Metropolitana.

Other awardees include the Partnership for Environmental Technology Education Community College Consortium for Health and Safety Training, whose members include Niagara and Ulster County

## NIEHS resources for Hurricane Sandy cleanup

NIEHS has the capacity to provide a basic four-hour safety and health awareness training program for cleanup and recovery workers. A booklet, presentations, and trainers are available to deliver the program in English or Spanish.

In New York state, labor law requires the provision of the OSHA 10-hour construction course to laborers, workers, and mechanics for any publicly funded construction project of at least \$250,000.

Upon request, representatives of NIEHS will meet with organizations to help identify needs and plan training. Following is a list of training that may be provided through NIEHS and its Clearinghouse:

- Hurricane Sandy site-specific hazard awareness
- Mold hazard awareness and mitigation techniques
- Respirator protection training
- Work zone safety
- Asbestos and lead awareness
- Defensive driving
- HAZWOPER operations and refresher
- OSHA 10 construction
- First aid, including cardiopulmonary resuscitation or automated external defibrillation
- Violence in the workplace

Many of the Hurricane Sandy training materials and additional information about the Clearinghouse are available at <http://tools.niehs.nih.gov/wetp/index.cfm?id=2472>

The hurricane booklet order form can be found at [https://tools.niehs.nih.gov/wetp/booklet\\_hurricane/index.cfm](https://tools.niehs.nih.gov/wetp/booklet_hurricane/index.cfm)

Community Colleges in New York, and the following union-based training organizations: International Union of Operating Engineers; Laborers' International Union of North America; International Brotherhood of Teamsters; Center to Protect Workers' Rights—Center for Construction Research and Training; Service Employees International Union; Civil Service Employees Association, Local 1000 in Albany, N.Y.; American Federation of State, County and Municipal Employees; and International Association of Fire Fighters.

[Return to Table of Contents](#)



*OSHA trainer Robert Ortiz, center, prepared a demonstration during a training session for members of the National Day Laborer Organizing Network Dec. 16, 2012, in Union Beach, N.J., one of the workshops conducted under existing contracts with members of the New York-New Jersey Consortium. WETP Public Health Educator Ted Outwater was also onsite for the Sunday afternoon workshop. (Photo courtesy of Ted Outwater)*

## Hrynkow named to head network of viral specialists

*By Eddy Ball*

Former NIEHS Associate Director Sharon Hrynkow, Ph.D., was appointed in December 2012 as president of the nonprofit [Global Virus Network \(GVN\)](#) of Baltimore. Prior to joining GVN, Hrynkow served as counselor and senior scientist in the Office of the Science and Technology Adviser to the U.S. Secretary of State and as senior advisor to the Assistant Secretary of State for Oceans and International Environmental and Scientific Affairs from 2010 to 2012. She also held leadership positions at NIH from 2000 to 2009.

According to a [GVN press release](#) announcing her appointment, Hrynkow will grow and diversify the organization's funding base, forge new ties with public and private sector groups, and work with international scientific teams to implement research and training paradigms to meet GVN goals. Among her first priorities are the expansion of fellowship and exchange programs among GVN's 30 centers of excellence in more than 20 countries, and the establishment of seed funding for innovative and international collaborative projects on high-risk pathogens.

"The need for a Global Virus Network linking the world's greatest medical virologists is urgent," Hrynkow was quoted as saying in the press release. "This is a time when the global community is becoming increasingly aware of the need for biomedical research and training in order to combat pandemic threats from viral disease. I could not be more thrilled to be asked by Bob Gallo and his esteemed colleagues to lead the GVN at such a critical time."



*Among Hrynkow's honors and awards are the Presidential Rank Award for Senior Executive Service and Royal Norwegian Order of Merit Award, as well as her election as a fellow of the American Association for the Advancement of Science (AAAS), chairperson of the AAAS Committee on Science, Engineering, and Public Policy, and member of the Council on Foreign Relations. (Photo courtesy of Steve McCaw)*



## Recognizing viral diversity and the need for a unified front

GVN was founded in 2011 by former National Cancer Institute lead researcher [Robert Gallo, M.D.](#), who became world famous in 1984 when he codiscovered the human immunodeficiency virus (HIV) as the cause of AIDS and developed the HIV blood test. In the years that followed his discovery, Gallo became increasingly convinced of the urgency of better understanding the more than 40 known classes of viruses that commonly infect humans. An important goal for him became more effectively supporting scientific collaboration and communication among experts worldwide.



“Since HIV/AIDS first appeared, I have strongly believed mankind will best be served if the world’s leading virologists are organized and better-equipped to deal with new and existing viral threats,” Gallo said of the new network of virus specialists. GVN is comprised of centers of excellence in medical virology worldwide, each directed by a recognized expert in human viral diseases, including the [Institute of Human Virology](#) at the University of Maryland School of Medicine, where Gallo has served as founding director since 1996.

## Hrynkow at NIH

In her position at NIEHS from 2007 to 2009, Hrynkow served as global health lead and principal liaison with NIH in Bethesda, Md., as well as other U.S. government agencies, non-governmental organizations, and foreign governments with offices in Washington, D.C. She also helped raise awareness of the value of women scientists in the field of biomedical research, both in the U.S. and abroad (see text box).

Prior to her appointment at NIEHS by then Acting Director Samuel Wilson, M.D., Hrynkow served as deputy director of the NIH Fogarty International Center (FIC) from 2000 to 2007, and acting director of FIC from 2004 to 2006. FIC serves as a bridge between NIH and the greater global health community, by facilitating exchanges among investigators, providing training opportunities, and supporting promising research initiatives in developing countries to help build capacity for improving global health.

Hrynkow has also advised numerous nonprofit groups with an interest in global health, including Medical Missions for Children, the American Association for the Advancement of Science, and the Institute of Medicine’s Roundtable on Environmental Health Sciences, Research, and Medicine.

[Return to Table of Contents](#)

### A selection of newsletter stories about Hrynkow’s work at NIEHS

- January 2008 — [Leadership and Gender Symposium for Latinas](#)
- April 2008 — [RAISE Recognizes the Contribution of Women Scientists](#)
- April 2008 — [NIEHS Marks International Women’s Day](#)
- July 2008 — [Homeschoolers Expand Their Understanding of Climate Change](#)
- August 2008 — [Hrynkow Addresses Embassy Science Officers](#)
- October 2008 — [Virtual Environmental Training for Latin American Women](#)
- December 2008 — [Hrynkow Chosen as AAAS Committee Chair](#)
- January 2009 — [NIEHS Represented at EcoHealth Conference](#)
- April 2009 — [NIEHS Women at Center Stage in Bethesda](#)
- July 2009 — [Hrynkow Honored for Mentoring](#)

# NIEHS opens search for clinical director

In January, NIEHS launched a search for a [director of the clinical research](#) program at the senior investigator, tenure-eligible level, with a closing date of Feb. 28.

The successful candidate will oversee current studies and develop new directions for the NIEHS [clinical and translational research program](#) at the [Clinical Research Unit](#) in Research Triangle Park, N.C., as well as components at the [NIH Clinical Center](#) in Bethesda, Md. Along with leadership responsibilities, the director of clinical research will lead an independent laboratory group within the NIEHS Division of Intramural Research headed by Scientific Director [Darryl Zeldin, M.D.](#)

Candidates must have a Doctor of Medicine or Doctor of Osteopathy degree and be board certified or board-eligible in a medical specialty approved by the American Board of Medical Specialties, with the ability to obtain medical licensure in the United States. Candidates should have an established and nationally or internationally recognized record in the conduct and supervision of clinical research in a discipline relevant to the environmental health sciences, as well as an established record of experience with clinical training, institutional review boards, and compliance with current clinical safety and regulatory issues.

Potential applicants can learn more about this career opportunity by visiting [http://niehs.nih.gov/careers/jobs/director\\_clinical\\_research\\_program\\_dir\\_1301.cfm](http://niehs.nih.gov/careers/jobs/director_clinical_research_program_dir_1301.cfm) or by contacting the designated NIEHS representative:

Ms. Emily Starnes (Vacancy Number DIR 13-01)  
Intramural Program Specialist  
National Institutes of Health  
National Institute of Environmental Health Sciences  
P.O. Box 12233, Maildrop A2-06  
Research Triangle Park, NC 27709  
Email: [dir-appls@niehs.nih.gov](mailto:dir-appls@niehs.nih.gov)

[Return to Table of Contents](#)

# Research fellow begins career in medical writing

*By Monica Frazier*

NIEHS research fellow Jeffrey Stumpf, Ph.D. began his new position Jan. 2 as a medical writer with MedThink SciCom in Raleigh, N.C. MedThink SciCom provides a range of scientific communication services for clients, including publication planning and writing; developing scientific platforms; and facilitating collaborations.

As a research fellow in the Mitochondrial DNA Replication Group in the Laboratory of Molecular Genetics headed by William Copeland, Ph.D., Stumpf characterized mutations in DNA Pol Gamma found in patients with mitochondrial disease, using yeast as an effective tool to test mitochondrial DNA replication *in vivo*. This work gave him the opportunity to communicate his research in a variety of ways, which he said was instrumental in his career path.

## NIEHS career development support

The transition from bench scientist to his new role as a medical writer will be smoother because of experiences Stumpf gained through NIEHS. Extracurricular activities, such as volunteering to give a talk on DNA and mutations to a general audience — an opportunity advertised at a seminar he attended — helped him realize his goal of effectively communicating science to various audiences ([see story](#)).

With Copeland's support and encouragement, Stumpf made a habit of embracing other opportunities made available to NIEHS fellows to practice his communication skills, including giving talks at international and local conferences ([see story](#)), as well as in high schools.

NIEHS Office of Fellows' Career Development Director Tammy Collins, Ph.D., is in the unique position of being both the leader of career development at NIEHS and Stumpf's former labmate. Collins explained that embracing the available career support at NIEHS as Stumpf did is a great way to develop skills for any career path, particularly invaluable skills in such areas as leadership, management, and communication. Sometimes, these activities also help trainees discover new interests and connections.

"Because Jeff was proactive in taking advantage of opportunities at NIEHS, he ultimately discovered a talent and passion that may have otherwise remained latent," Collins observed.



*Stumpf first learned of newsletter writing opportunities at the 2010 NIEHS Biomedical Career Fair during a session on careers in science outreach. During the 2 ½ years he contributed to the NIEHS monthly newsletter, he built an impressive portfolio of writing samples for his job search. (Photo courtesy of Steve McCaw)*

## The eFactor experience

Of all his non-bench activities, Stumpf was most passionate about his regular contributions to the Environmental Factor. He enjoyed the challenge of covering a variety of stories, including papers of the month, retirements, seminars, and awards. When asked about how writing for the newsletter changed his interests and career perspective, Stumpf said, "The foundation of my interest in scientific writing came solely from my experience in writing with the eFactor."

Before becoming an eFactor contributor, Stumpf's non-research interests centered on teaching. "When I started writing articles for the eFactor, I realized that I [also] enjoyed the challenge of communicating difficult and complex scientific topics in a coherent and even entertaining way," he explained.

Stumpf noted that the constant practice of writing articles on different topics helped him develop confidence in his writing. He was especially candid about the mentorship he received from newsletter editor Eddy Ball and other members of the Office of Communications and Public Liaison, crediting their support with playing an important role in his decision to consider writing as a career option.

"Eddy inspired me to continue on this path and ultimately convinced me that I can write about science for a living," Stumpf said.

(Monica Frazier, Ph.D., is an Intramural Research Training Award fellow in the NIEHS Mechanisms of Mutation Group.)

[Return to Table of Contents](#)



# Grantees elected fellows of AAAS

*By Eddy Ball*

Five NIEHS grantees will be among new fellows honored this year by the American Association for the Advancement of Science (AAAS). The scientists, who were elected as fellows in the Biological Sciences and Pharmaceutical Sciences sections, will receive a certificate and rosette Feb. 16 in Boston, during the AAAS Fellows Forum, which is part of the group's [annual meeting](#).

AAAS is the world's largest general scientific society and publishes the journal Science. Founded in 1848, the society includes more than 261 affiliated societies and academies of science, serving about 10 million individuals. A nonprofit organization, the society is open to all, and fulfills its mission to advance science and serve society through initiatives in science policy, international programs, and science education.

The [2012 AAAS Fellows](#) include the following distinguished scientists who enjoy support by NIEHS:

- [Michael Aschner, Ph.D.](#), was commended for distinguished contributions to the field of toxicology, particularly research on the mechanisms of metal in induced neurotoxicity. An NIEHS grantee since 1989, Aschner is professor of pediatrics and pharmacology and Gray E. B. Stahlman Chair in Neurosciences at the Vanderbilt University School of Medicine.

Aschner's laboratory focuses on the role of astrocytes in brain physiology and pathology, addressing the mechanisms of transport of methylmercury and manganese across the capillaries composing the blood-brain barrier, as well as their cellular and molecular mechanisms of neurotoxicity. Other studies address the basic interaction between genetics and environmental exposure to these metals in *C. elegans* and rodents.



*AAAS Fellow Aschner is shown in his lab.  
(Photo courtesy of Michael Aschner)*

- [Richard S. Pollenz, Ph.D.](#), was singled out for distinguished contributions to the field of molecular toxicology, particularly for advances in understanding aryl hydrocarbon receptor signal transduction at the protein level. An NIEHS grantee since 1997, Pollenz is a professor, associate dean for undergraduate studies, and director of the Office for Undergraduate Research at the University of South Florida.

In addition to his bench research, he has developed innovative strategies to enhance undergraduate research, including an initiative that allowed 600 students to receive research experience through their coursework in 2012, and has received awards for innovations in teaching for the use of music and karaoke to understand key science concepts.



*AAAS Fellow Pollenz (Photo courtesy of  
Richard Pollenz)*

- **Alvaro Puga, Ph.D.**, was named an AAAS Fellow for his contributions to the field of environmental genetics. Puga is a professor in the University of Cincinnati (UC) College of Medicine's top-ranked environmental health department and an associate director for the UC Center for Environmental Genetics. An NIEHS grantee since 1996, he is considered by colleagues in his field to be the pioneer in the use of molecular biology to study the biological responses to toxic insult.

Puga was honored by the UC Department of Environmental Health with the Director's Award for Excellence in Research, as well as with faculty and teaching awards from his department and the UC College of Medicine.



*AAAS Fellow Puga (Photo courtesy of Alvaro Puga)*

- **Michael Skinner, Ph.D.**, was recognized for his distinguished contributions to mammalian reproduction and environmental epigenetics, and discovering environmental effects on gonadal development causing epigenetic transgenerational inheritance of adult-onset disease with potential impacts in medicine and evolution.

Skinner is a professor in the School of Biological Sciences at Washington State University and an NIEHS grantee since 2005. He established, and has been the director of, the Washington State University and University of Idaho Center for Reproductive Biology, one of the largest reproductive sciences research centers in the world, since its inception in 1996. He also established and was the director of the Center for Integrated Biotechnology until 2008.



*AAAS Fellow Skinner (Photo courtesy of Washington State University)*

- **John Stamatoyannopoulos, M.D.**, was honored for his contributions to the field of genome sciences. He is an associate professor of genome sciences and medicine at the University of Washington and an NIEHS grantee since 2008.

Stamatoyannopoulos made several major contributions to the ENCODE project, an international effort to understand the regulatory elements of the human genome. He developed powerful techniques for mapping these complex control networks, which turn out to have patterns similar to those found in primitive brains. Through a greater understanding of the role of genome regulators generated in his lab, new ways of looking at the causes and progression of disease are likely to emerge.



*AAAS Fellow Stamatoyannopoulos is shown in his lab. (Photo courtesy of John Stamatoyannopoulos)*

# Outreach educator honored with SOT Public Communications Award

*By Ed Kang*

NIEHS grantee Marti Lindsey, Ph.D., has been honored with the 2013 Society of Toxicology (SOT) Public Communications Award. Her recognition stems from her efforts to develop and disseminate environmental health materials specifically related to issues of concern in the southwestern U.S.

Lindsey is the director of the Community Outreach and Education Core (COEC) of the Southwest Environmental Health Sciences Center (SWEHSC). The center is an NIEHS Environmental Health Sciences Core Center located at the University of Arizona (UA).

Lindsey has become nationally recognized for her success with outreach and communication with Native American populations in Arizona. Her efforts to communicate the hazards of relevant contaminants in local communities, such as the Gila River Indian Community and the Inter Tribal Council of Arizona, have had significant impact and fostered collaborations that address wide-ranging health disparities.

“She is a nationally recognized leader in the development of interactions with, and dissemination of information to, the native community,” said Clark Lantz, Ph.D., SWEHSC deputy director and associate head of cell biology and anatomy at UA. “The impact that she has had on communicating important environmental information to the public is immeasurable.”

Under Lindsey’s guidance, the COEC develops materials related to SWEHSC research topics, such as arsenic exposure, asthma, lead poisoning, and skin cancer from ultraviolet exposure, as well as other health issues related to air toxics, water contamination, pesticides, and hazardous waste. To support the outreach effort, she has led the creation and dissemination of successful flyers, information walks, presentations, and Web materials.

Nathan Cherrington, Ph.D., director of graduate studies in the UA department of pharmacology and toxicology, remarked, “I can quite confidently say that no single person has done more to extend environmental health education in the state of Arizona than Marti. Her work and influence is meaningful to the public in general but, more importantly, has benefited the underserved and Native American populations of the state. “

The Public Communications Award is presented by SOT to recognize an individual who has made a major contribution to broadening the awareness of the general public on toxicological issues through any aspect of public communications.

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)



*As a member of the Navajo Nation, Lindsey is directly invested in Native American health and outreach. By tirelessly reaching out to these communities, she has built successful partnerships based on trust. (Photo courtesy of Marti Lindsey)*

[Return to Table of Contents](#)



## New logo emphasizes NIH identity

What's that new symbol on the home page? The new NIH logo. The logo was developed over the past year as part of a larger effort to strengthen the impact of NIH communications. It responds to

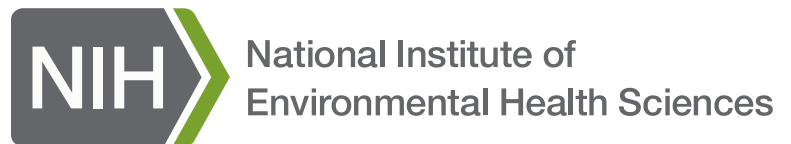
a growing clamor among NIH constituents — from members of Congress and from NIH's own leadership — that the agency needs to communicate with maximum impact the value of investing in biomedical research.



“Now, more than ever, it's time to make the strongest case possible that NIH has a profound, positive influence on people's lives every day,” said John Burklow, NIH associate director for communications and public liaison. “We also need to make it as easy as possible for the public to understand the full scope of NIH's work. We need to start by becoming less fragmented and more focused in our communications.”

The logo was formally adopted by the institute and center directors and NIH leadership last November after much consultation internally and externally. They decided it was best to go with a clean, “mobile device-friendly” design that features the letters “NIH,” consistent with a growing trend in logo design.

They also agreed that it will be the only “visual mark” to be used across the agency to reduce confusion for the public. The institutes, centers, offices and programs will be identified by text added in the space after or under the arrow.



For the historians among us, the new logo appeared officially on the home page on Nov. 29, 2012, as only the fourth mark to be used by NIH in its history. Use of the new logo is being phased in gradually and in a cost-conscious way.

In addition to the new, consistent visual identity, NIH is stepping up its efforts to work with grantees to make clear that their work is made possible through support from NIH. Some 84 percent of NIH funding goes outside the agency to thousands of institutions around the country. This is sometimes, surprisingly, a little-known fact outside the Bethesda campus.

Also, there will soon be a “toolkit” available to institutes and centers. It will contain resources to communicate about NIH, including detailed visual identity guidelines, PowerPoint slides, talking points and best practices for engaging grantees, patient and voluntary organizations, professional societies and the interested public.

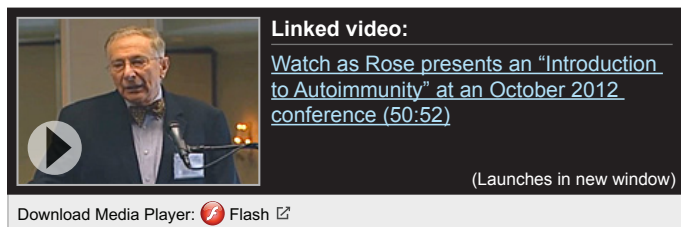
[Return to Table of Contents](#)

# Science Notebook

## Autoimmunity expert delivers distinguished lecture

By Sheetal Thakur

NIEHS opened its 2012-2013 Distinguished Lecture series with a seminar on autoimmune diseases, disorders caused by a person's immune system erroneously attacking its own healthy tissues. Noel Rose, M.D., Ph.D., a leading autoimmunity expert, came to NIEHS Jan. 8 and presented "Myocarditis: an environmentally induced autoimmune disease." [Dori Germolec, Ph.D.](#), head of the Systems Toxicology Group in the NTP Toxicology Branch, hosted the event.



*"The most disturbing aspect is that the incidences of autoimmune disorders are going up," Rose said. "It is really an environmental problem, and it's going to get worse unless we pay attention to it."*  
(Photo courtesy of Steve McCaw)

[Rose](#) is a professor of molecular microbiology and immunology and director of the Center for Autoimmune Disease Research at Johns Hopkins Bloomberg School of Public Health. During Germolec's introduction, she described Rose as one of the founding fathers of immunology and autoimmunity research. She particularly emphasized his early pioneering discoveries in which he and his colleagues were the first to model Hashimoto's thyroiditis, an autoimmune disease that causes chronic inflammation of the thyroid gland, in a number of species ranging from chickens to primates. She listed awards from his impressive list of accomplishments, and praised his outstanding mentorship record of guiding approximately 120 students and postdoctoral fellows during his career.

Rose's laboratory focuses on elucidating the commonalities that underlie various autoimmune diseases. Early in his talk, he emphasized that seemingly diverse autoimmune diseases belong to the same family and have many common genetic traits and environmental triggers. He explained that these common traits determine whether an organism will be susceptible or resistant to developing autoimmune disorders.

"If we are ever going to find a way of actually curing an autoimmune disease," Rose remarked, "I believe it is going to come from our understanding of what those common traits are."



[Fred Miller, M.D., Ph.D.](#), left, acting director of the NIEHS Clinical Research Program and head of the Environmental Autoimmunity Group, shared Germolec's enthusiasm about the lecture. (Photo courtesy of Steve McCaw)

## Environmental triggers to autoimmune myocarditis

According to Rose, viral myocarditis is usually a self-limiting disease, with most of the affected people completely recovering without showing any outward appearance of the disease. The condition may develop into an autoimmune disorder in a few individuals. Autoimmune myocarditis is usually manageable with medication, unless it progresses to a fibrotic state in the heart known as dilated cardiac myocarditis (DCM). The only cure for DCM is heart replacement. Rose and his group have previously demonstrated that environmental chemicals and agents, such as inorganic mercury and bacterial lipopolysaccharide, intensify the virally induced autoimmune myocarditis and DCM.



*Postdoctoral fellows from the Laboratory of Signal Transduction, left to right, Diana Cruz, Ph.D., Mahita Kadmiel, Ph.D. and Sivapriya Ramamoorthy, Ph.D., also said they enjoyed the seminar. (Photo courtesy of Steve McCaw)*

## Cytokines and autoimmune myocarditis

Rose uses different strains of mice, with varying susceptibility, to investigate the role of inflammatory cells and cytokines in progression from initial virus infection to a heart-specific autoimmune disease. In murine models, autoimmune myocarditis can be initiated by infection with coxsackievirus B3 or by immunizing with cardiac myosin.

Rose discussed the influence of effector T-cell subpopulations and different cytokines in autoimmune cardiac inflammation and progression to DCM. He mentioned that all three effector T-cell pathways Th1, Th2, and Th17 are important, and their relative involvement determines disease outcome. He discussed findings from his laboratory, which demonstrated the crucial roles that two cytokines with different mechanisms — interferon-gamma (IFN-gamma) and interleukin 17 (IL-17) — play in the progression from initial viral infection to DCM and death. IFN-gamma is involved in reducing the severity of the inflammatory response, while IL-17 is essential for progression to the fatal fibrotic DCM.

Rose concluded his talk by saying that, at present, autoimmune diseases cannot be cured, but they can potentially be prevented.

“The most efficient way of preventing autoimmune diseases would be by identifying and separating the susceptible human from the responsible environmental factor,” he said.

(Sheetal Thakur, Ph.D., is an Intramural Research Training Award fellow in the NTP Toxicology Branch.)

[Return to Table of Contents](#)

## Nano meeting tackles consumer exposures

*By Eddy Ball*

An impressive lineup of speakers at the NIEHS Nano Exposure Workshop Jan. 9-10 underscored how much scientists still don't understand about the health effects of engineered nanomaterials (ENMs), more than a decade after studies of their toxicology first began to appear in the PubMed-indexed literature.



The latest in a series of initiatives led by NIEHS to advance understanding of nanomaterials (see text box), the workshop was organized by NIEHS program administrator [Sri Nadadur, Ph.D.](#), who manages the nano grants portfolio. The goal of the workshop was to initiate a discussion with researchers in the fields of nanomaterial science, toxicology, exposure assessment, consumer protection, and epidemiology, to prioritize the research directions for gaining comprehensive understanding of potential health effects from nano-enabled consumer products. Welcoming remarks by NIEHS [Deputy Director Rick Woychik, Ph.D.](#), emphasized the urgent need to understand how these materials may interact and contribute to health effects, as the number of products containing nanomaterials continues to increase at a rapid pace.

“I think [it’s important] having all the parts of the health research spectrum represented here and talking together,” said participant Carolyn Cairns, program leader for product safety at Consumers Union. “Now we’re [specifically] talking about product-related exposure.”

### Keynote sets the tone for panel discussions

Addressing “Progress towards predicting environmental exposure to engineered nanomaterials” was one of the field’s leading authorities, environmental engineer [Mark Wiesner, Ph.D.](#), director of the Duke University Center for the Environmental Implications of NanoTechnology. Wiesner described advances in nano research that seem to raise as many questions as answers, especially about what happens as the relatively stable products change and break down during the course of their life cycles.



NIEHS leadership at the meeting included Woychik, left, who welcomed attendees and discussed the role nano research plays in the NIEHS strategic plan, and Collman, who looked forward during her closing remarks. (Photo courtesy of Steve McCaw)

## NIEHS gives nano research a big push forward

Along with individual researcher-initiated grants, NIEHS nanotechnology Grand Opportunities (Nano GO) grants gave researchers two years of funding ([see story](#)) for grantees to work together toward the common goal of developing methods to achieve greater harmonization of research results for hazard assessment of ENMs. The consortium researchers conducted several collaborative research projects, structured as a series of round-robin tests, in which similar or identical methods were used to perform *in vitro* and *in vivo* tests concurrently at thirteen different laboratories around the country.

The NIEHS Centers for Nanotechnology Health Implications Research (NCNHIR) Consortium, formed in 2010, consisted of eight cooperative centers along with several other active grantees funded through the Nanotechnology Environmental Health and Safety program ([see story](#)). NIEHS also established contractual agreements with the Nanotechnology Characterization Laboratory for nanomaterial characterization, and with the National Institute of Biomedical Imaging and Bioengineering to create an informational database.

During its two years of funding, NCNHIR supported opportunities for grantees through NIEHS programs, including Nano GO, Challenge Grants, Outstanding New Environmental Scientist (ONES), and research project grants, to share and integrate data. The interactions among nano scientists laid the foundation for the kinds of cooperative efforts and interagency partnerships fostered by the Nano Exposure Workshop.

“It’s important to understand the uncertainties,” Wiesner told the audience. In the world of nano-scaled metals and elements, Wiesner explained, structure-related peculiarities explain only part of ENM behavior and potential impact on health. Manufacturing conditions, mixtures, and interactions with the environment, along the course of the material’s life cycle, can alter the material and influence its exposure and risk potential.

### Spheres of agreement

The workshop was divided into four sessions, each with a set of major questions to guide panel presentations and discussion — nano environmental health and safety, tools for nano exposure assessment, consumer exposure to ENMs, and knowledge and needs for epidemiology of ENM exposures.

In any gathering of toxicologists, exposure biologists, epidemiologists, and researchers from other disciplines, there are bound to be points of contention, but there was a remarkable level of consensus about several issues. It remains unclear what the exact volume of ENMs is in production, what products contain them, or how ongoing research and development will change their character in the future — something that expanding public-private partnerships may help address.

Initial studies of exposure in occupational settings are only now getting underway, laboratory characterization of nanomaterials is early in development, and epidemiologists struggle with questions about where to begin in the design of the large population studies that are sorely needed to define exposure and forecast risk. Understanding the fate of ENMs, after they enter the body through inhalation, ingestion, and dermal exposure, remains incomplete.

Even the research infrastructure, several speakers observed, is still inadequate. The National Health and Nutrition Examination Survey (NHANES) — a major resource for environmental health studies and public health efforts — doesn’t yet analyze tissue samples for nanomaterials, researchers still struggle with characterization, and the National Library of Medicine is still in the process of expanding its PubMed index and other database coverage of nano research.

### Moving forward with partnerships

In her final remarks to the attendees, NIEHS Director of the Division of Extramural Research and Training [Gwen Collman, Ph.D.](#), spoke encouragingly of the spirit of cooperation evident throughout the workshop.



*Shortly after he began his keynote address, Wiesner, right, abandoned the podium for more intimate engagement with the audience. He was joined by Nadadur during the question and answer segment. (Photo courtesy of Steve McCaw)*



*EPA scientist [Kevin Dreher, Ph.D.](#), led off the first session with a discussion of “ENMs risk assessment: health effects primer.” In his review of health effects research, he said, “There are many confounding factors. Those things [ENMs] change as they go through the environment.” (Photo courtesy of Steve McCaw)*



She pointed to offers to share samples and assessment platforms; proposals for cross-disciplinary teams with specialists in toxicology, exposure assessment, and epidemiology; advancing strong interagency partnerships; and the prospect of novel partnerships with private sector stakeholders.

Several attendees stayed on after the workshop to participate in the NIEHS-hosted Nanomaterials Characterization Workshop organized by [ILSI](#) and the University of Michigan Risk Science Center.



*Contrasting the workshop experience with the state of the science that informed her 2006 [testimony](#) before a U.S. Food and Drug Administration panel, Cairns said she felt hopeful about advancing understanding of exposure and risk in the general population. (Photo courtesy of Steve McCaw)*



*[Consumer Product Safety Commission](#) toxicologist Treye Thomas, Ph.D., moderated the consumer product session. He said such products drive exposures among children and other susceptible groups. (Photo courtesy of Steve McCaw)*



*Richard Canady, Ph.D., right, director Center for Risk Science Innovation and Application at ILSI, was one of the co-organizers of the Nanomaterials Characterization Workshop that followed the exposure meeting, while grantee [Terry Kavanagh, Ph.D.](#), of the University of Washington, was a panelist in the session on nano environmental health and safety. (Photo courtesy of Steve McCaw)*



*Grantee [Martin Philbert, Ph.D.](#), dean of the University of Michigan School of Public Health, right, commented on Wiesner's description of life-cycle modifications of ENMs. "All these properties change as you go from system to system," he said. NIEHS program administrator Caroline Dilworth, Ph.D., left, organized and moderated the epidemiology panel. (Photo courtesy of Steve McCaw)*





NIEHS program administrator [David Balshaw, Ph.D.](#), left, moderated the tools session, which included discussion of some of the personal sensors developed with grants he oversees. National Institute for Occupational Safety and Health project leader Laura Hodson, right, described ongoing industry-wide occupational exposure assessment [studies](#) by her group, funded in part by NTP. (Photo courtesy of Steve McCaw)



NTP Deputy Director for Science [Nigel Walker, Ph.D.](#), helped to ground the nano environmental health and safety session with his presentation on “Classical risk assessment paradigm.” (Photo courtesy of Steve McCaw)



Bethesda-based NIEHS Toxicology Liaison [Chris Weis, Ph.D.](#), was on hand for the workshop and represented NIEHS at the Nanomaterials Characterization Workshop that followed. (Photo courtesy of Steve McCaw)



Offering an example of the cross-disciplinary cooperation nurtured by the workshop, grantee [Mary Wolff, Ph.D.](#), right, an epidemiologist at Mount Sinai Medical Center, took advantage of a break to talk with environmental biomarker specialist [Justin Teeguarden, Ph.D.](#), of Pacific Northwest National Laboratory. (Photo courtesy of Steve McCaw)



Although most of the evidence suggests ENMs do little harm as they pass through the gastrointestinal tract, grantee James Bonner, Ph.D., of North Carolina State University noted a possible exception. Because of its antimicrobial properties, silver could impact healthy balance of flora in the microbiome. (Photo courtesy of Steve McCaw)

# NIEHS researcher assists in study of Norwegian women

By Robin Arnette

Norwegian pregnant women who received a vaccine against the 2009 H1N1 influenza virus showed no increased risk of pregnancy loss, while pregnant women who experienced influenza during pregnancy had an increased risk of miscarriages and still births, a new [study](#) has found. The study suggests that influenza infection may increase the risk of fetal loss.

Scientists from NIEHS and the [Norwegian Institute of Public Health \(NIPH\)](#) published their findings online Jan. 17 in the New England Journal of Medicine. The research was conducted following the H1N1 influenza pandemic that took place between spring 2009 and fall 2010.

Norwegian public health officials had urged pregnant women to be vaccinated. However, media reports of pregnancy losses after flu shots caused some expectant mothers to forgo vaccination.

First author Siri Haberg, M.D., Ph.D., of NIPH, and colleagues initiated the study to help address the question of vaccine safety, by taking advantage of Norway's excellent registries and medical records system. Haberg spent one year of her postdoctoral fellowship in the NIEHS Epidemiology Branch before returning home to Norway during the pandemic.

NIEHS researcher and co-author [Allen Wilcox, M.D., Ph.D.](#), said the NIPH researchers combined data from obstetrical visits, birth records, and vaccination registries to investigate whether the influenza vaccination posed a risk to pregnancy. The study found that influenza infection increased the risk of fetal loss by up to twofold. Influenza vaccination did not increase the risk of loss. Instead, the results suggest that vaccination reduces the risk of fetal loss.

"Most important is that vaccinations protect pregnant women against influenza illness, which could be harmful for both the mother and the baby," Wilcox said. "If pregnant women are worried about their fetus, then getting a flu shot is a good thing to do."

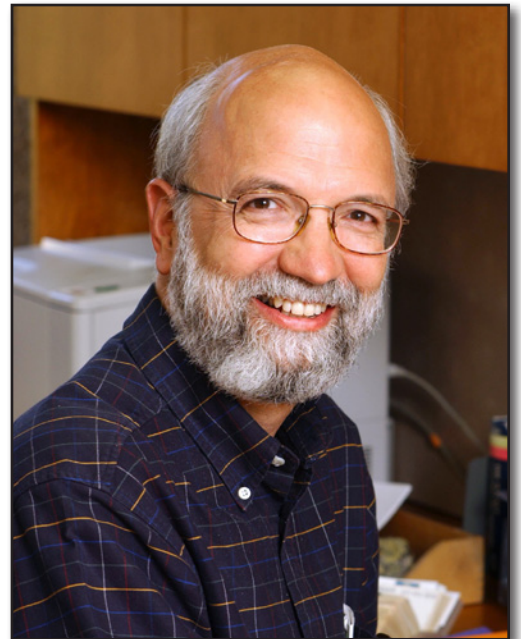
Haberg added, "Pregnant women should find it reassuring that we found no harmful effects on the fetus associated with H1N1 vaccination."

*Citation:* [Haberg SE, Trogstad L, Gunnes N, Wilcox AJ, Gjessing HK, Samuelsen SO, Skrondal A, Cappelen I, Engeland A, Aavitsland P, Madsen S, Buajordet I, Furu K, Nafstad P, Vollset SE, Feiring B, Nokleby H, Magnus P, Stoltenberg C.](#) 2013. Risk of fetal death after pandemic influenza infection or vaccination. N Engl J Med; doi:10.1056/NEJMoa1207210 [Online 16 January 2013].

[Return to Table of Contents](#)



*Haberg and her NIPH colleagues began gathering data for this study in 2010. She was at NIEHS from 2008 to 2009. (Photo courtesy of Steve McCaw)*



*Wilcox heads the Reproductive Epidemiology Group in the NIEHS Epidemiology Branch. He was the only American on the Norwegian team. (Photo courtesy of Steve McCaw)*



# Exploring the haunting legacy – benomyl and Parkinson's

By Sheila Yong

More than a decade after the use of the fungicide benomyl was discontinued in the U.S., its toxic effects are still fresh in the minds of an interdisciplinary team of researchers at the University of California, Los Angeles (UCLA). Their latest NIEHS-funded [research](#) reports on the discovery of a mechanism involved in Parkinson's disease (PD) that results in the inhibition of a key enzyme in the brain and may offer insight into a novel treatment approach.

In a study published in the Jan. 8 edition of the journal *Proceedings of the National Academy of Sciences*, the researchers reported that benomyl exposure results in damage of the dopaminergic neurons in the brain. The study was led by senior author [Jeff Bronstein, M.D., Ph.D.](#), whose laboratory is part of the NIEHS Centers for Neurodegeneration Science (CNS) program.

Researchers at the CNS at UCLA have been devoting their efforts to uncovering the link between pesticides and the pathologies of PD. They had previously found an association between pesticide exposure and increased risk of PD in a well-established patient cohort in the agricultural region of California's Central Valley. Besides conducting epidemiological studies involving human subjects, the researchers also utilized cell culture and animal models to dissect the mechanisms involved in PD development.

## Not just a genetic problem

As the name implies, dopaminergic neurons are the main source of the neurotransmitter dopamine. These neurons are important in many brain functions, including voluntary movement and a variety of behavioral processes. Damage to these neurons is often associated with PD.

While research on PD has revealed genetic mutations that contribute to the inherited form of the disease, these mutations only account for a small fraction of disease occurrence, said first author of the study and a postdoctoral scholar in Bronstein's laboratory Arthur Fitzmaurice, Ph.D., in a UCLA [press release](#). "As a result, environmental factors almost certainly play an important role in this disorder. Understanding the relevant mechanisms, particularly what causes the selective loss of dopaminergic neurons, may provide important clues to explain how the disease develops," he added. One such environmental factor is the wide use in the 1970s of benomyl, which has the potential to cause liver tumors, brain malformations, reproductive defects, and carcinogenesis.

To establish a direct causal relationship between benomyl and PD, the researchers turned to primary neuronal cultures and zebrafish embryos to see if benomyl could cause any of the PD pathologies in these experimental systems. They found that benomyl selectively damaged the dopaminergic neurons, while leaving the other neurons unscathed. Interestingly, the researchers also observed a swimming deficit in zebrafish exposed to benomyl, suggesting that the loss of dopaminergic neurons resulted in impaired voluntary movement in these organisms.



*Fitzmaurice is a postdoctoral scholar working in the Bronstein group under an NIEHS training grant. (Photo courtesy of Randy Guaiya)*



## An inhibited enzyme points to a potential target for treatment

Based on their previous finding that benomyl inhibits aldehyde dehydrogenase (ALDH) activity in mouse mitochondria, the authors sought to determine if ALDH activity was also inhibited in benomyl-treated primary neurons. Through fluorescence-based enzyme activity measurements, they found that benomyl inhibited ALDH activity in the neurons and its effect was concentration-dependent.

ALDH is required to metabolize dopamine metabolite 3,4-dihydroxyphenylacetaldehyde (DOPAL), which is toxic to the brain and has been proposed to contribute to PD development. Hence, the authors proposed that ALDH inhibition and the subsequent accumulation of DOPAL lead to an increased risk in developing PD.

This study unveils a novel mechanism for PD development, which involves the inhibition of ALDH, making it potentially a novel target for drug therapy, according to Bronstein. The authors did not observe any connection between benomyl exposure and accumulation of alpha-synuclein, which, until now, had been considered the central driver of PD pathogenesis.

More importantly, findings from this study reinforce the authors' hypothesis that pesticides may be partially responsible for the high PD occurrence rates among farmers and others in rural areas. "The discovery of this new pathway may be a new avenue for developing therapeutic drugs," Bronstein said.

*Citation:* Fitzmaurice AG, Rhodes SL, Lulla A, Murphy NP, Lam HA, O'Donnell KC, Barnhill L, Casida JE, Cockburn M, Sagasti A, Stahl MC, Maidment NT, Ritz B, Bronstein JM. 2013. Aldehyde dehydrogenase inhibition as a pathogenic mechanism in Parkinson disease. *Proc Natl Acad Sci U S A*. 110(2):636-641.

(Sheila Yong, Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction.)

[Return to Table of Contents](#)



*Bronstein is a professor of molecular toxicology and neurology and is director of the Movement Disorders Program at UCLA. (Photo courtesy of UCLA)*

## PEPH launches new podcast series

*By Rayna Rowell*

Researchers, working in partnership with community groups, are featured in a new podcast series by the NIEHS [Partnerships for Environmental Public Health](#) (PEPH) program. PEPH launched its new podcast series, [Environmental Health Chat](#), Jan. 14.

"The goals of the Environmental Health Chat series are to highlight NIEHS-funded community-engaged research projects and to spread the word about important and emerging environmental public health issues to a wide audience," said Liam O'Fallon, PEPH program coordinator.

## Straight to the point

The short podcasts focus on one or two key messages of a featured topic. To supplement each podcast, the page has links to relevant resources and references. The first four podcasts are now available, with plans to release a new podcast every month starting in February.

[Hydraulic fracturing](#) (fracking) was the subject of one podcast featuring [Roxana Witter, M.D.](#), of the Colorado School of Public Health. Witter provided background information about fracking and offered [health impact assessment](#) as a useful tool for evaluating the potential effects of a drilling operation on a community.

Another podcast, featuring Brown University Superfund Research Program (SRP) grantee [Phil Brown, Ph.D.](#), and Environmental Justice League of Rhode Island Director [Amelia Rose](#), highlighted a new [school siting law](#). They discussed issues with schools being built in or near areas with known contamination. In addition to outlining the potential health effects of this practice, they also examined the environmental justice implications.

[R. William Field, Ph.D.](#), a professor at the University of Iowa, discussed [radon](#) and its health effects in a third podcast. Field emphasized that radon is the leading environmental cause of cancer death in the United States. This podcast gave an overview of radon and provided steps to take to reduce exposure.

The last podcast featured [Celia Chen, Ph.D.](#), a Dartmouth Toxic Metals SRP grantee, discussing [mercury in seafood](#). Chen explained how mercury gets into the food chain and what types of fish are safe to eat to reduce exposure.

## Feedback and ideas

PEPH invites scientists, community-based participatory researchers, and the general public to visit the Environmental Health Chat page and provide feedback, as well as ideas for future podcasts. Next month, there will be a podcast on urban gardening that will highlight research from Cornell University.

(Rayna Rowell is a communication specialist with MDB, Inc., a contractor for the NIEHS Division of Extramural Research and Training.)

[Return to Table of Contents](#)

# Air pollution pinpointed as major global health problem

*By Nancy Lamontagne*

Findings from the [Global Burden of Diseases, Injuries, and Risk Factors Study \(GBD\) 2010](#) underscore the conventional wisdom that air pollution is a major health risk factor across the globe. The study also shows that noncommunicable diseases, such as cancer and heart disease, are now the main causes of death and disability worldwide.



*"With this podcast series, PEPH complements its [PEPH eNews](#) and [webinar series](#), as tools for reaching and engaging a diverse audience," O'Fallon said. (Photo courtesy of Steve McCaw)*

GBD 2010, a large global health project, systematically examined the global distribution and causes of major diseases, injuries, and health risk factors.

“The study showed that global particulate matter pollution is a major avoidable risk to the health of humankind,” said NIEHS grantee [George Thurston, Sc.D.](#), of New York University Langone Medical Center, and co-author on three of the [seven GBD 2010 papers](#) published December 2012 in The Lancet. “A high policy priority must be to reduce sources of particulate matter air pollution,” argued Thurston.

### Air pollution, life expectancy, and quality of life

Thurston, who served on the GBD Outdoor Air Pollution Expert Group, pointed to the record high particulate matter (PM) air pollution Beijing experienced in January, along with recent [studies](#) linking increasing life expectancy in the U.S. with declining PM air pollution, as further proof of the importance of reducing air pollution around the world.

One GBD 2010 [paper](#) reported that indoor household and outdoor ambient PM air pollution have a large effect on diminished quality of life. Disability-adjusted life years (DALYs) assess disease burden, by combining the years of life lost and years lived with disability. Indoor household PM air pollution contributed to 4.5 percent DALYs, and outdoor ambient PM air pollution contributed to 3.1 percent. Together, indoor and outdoor PM contributed 7.6 percent DALYs, compared to blood pressure at 7.0 percent, tobacco smoking including second-hand smoke at 6.3 percent, and alcohol use at 5.5 percent.

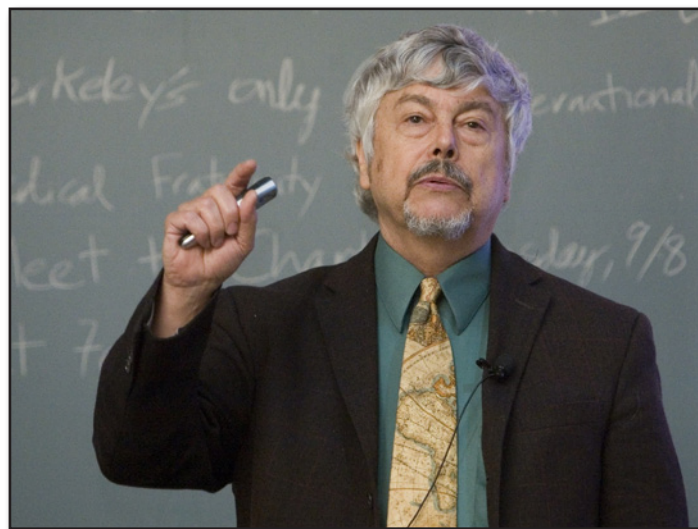
NIEHS grantee [Kirk Smith, Ph.D.](#), of the University of California, Berkeley, chaired the study’s Household Air Pollution Expert Group. “In terms of DALYs, household air pollution was the second most important risk factor for women and girls, globally, and the largest environmental risk factor of those examined,” he said. According to the study, household air pollution from solid cooking fuels directly caused 3.5 million premature deaths in 2010, and another half a million through its contribution to outdoor air pollution. The study relied heavily on the NIEHS-funded RESPIRE study in Guatemala for the impact of household air pollution on child pneumonia, which accounted for one-third of the total impact.

### Assessing rural air pollution

Thurston worked with other investigators to estimate global PM<sub>2.5</sub>, ozone exposures, and the health effects arising from pollution exposure. He points out that by including rural air pollution exposures, GBD 2010



*Thurston served on the Outdoor Air Pollution Expert Group for GBD 2010. (Photo courtesy of George Thurston)*



*As a champion for reducing global climate change and promoting environmental health, Smith shared the 2007 Nobel Peace Prize and earned the 2009 Heinz Award and 2012 Tyler Prize for achievements in environmental research. Smith has conducted pioneering studies of the health effects of indoor air pollution in homes that use inefficient cookstoves. (Photo courtesy of UC Berkeley)*



examined roughly double the population of GBD 1990. [New developments](#) made it possible to use satellite data to create global models that assess rural exposures. The estimates for the health impacts of PM2.5 and ozone made significant use of NIEHS-supported work in which Thurston examined the roles of pollution in cardiopulmonary mortality, lung cancer mortality, and substantial life-shortening.

“A pressing high priority research need is to assess which sources of particles are the most damaging — coal burning, traffic, biomass — so we can most cost-effectively reduce this public health threat,” Thurston said. Thurston and his colleagues are now working to identify the most dangerous PM sources in an NIEHS-funded study examining the effects of air pollution on the NIH-AARP Diet and Health Study cohort, which includes more than 500,000 people.

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

[Return to Table of Contents](#)

## Ho group uses saliva for study on methylation in asthma

*By Eddy Ball*

A new study by researchers at the University of Cincinnati Medical Center (UCMC) and the Cincinnati Children’s Hospital Medical Center (CCHMC), led by NIEHS grantee [Shuk-mei Ho, Ph.D.](#), has identified epigenetic changes associated with asthma in saliva samples. They report their results in a letter to the editor published online Dec. 20, 2012 in the *Journal of Allergy and Clinical Immunology*.

According to the authors, the study provides the first evidence that increased methylation of the promoters of the gene that encodes for forkhead box protein 3 (*FOXP3*) is associated with chronic exposure to diesel exhaust pollution (DEP) during childhood, and increased risk for persistent wheezing and asthma. The findings point to a less invasive and inexpensive procedure for collecting DNA that may become useful in the future for conducting large epidemiologic studies of children.

In addition, the authors conclude, “These findings support future strategies targeting [regulatory T] Treg cell expansion through boosting *FOXP3* upregulation for asthma prevention and intervention.”

### Downregulation of *FOXP3* and a dysregulated immune system

Ho and her colleagues constructed their hypothesis around the role of *FOXP3* expression in supporting normal function of Treg cells to suppress immune responses, including the airway inflammation response that becomes chronic in asthma, against such nonspecific stimuli as DEP. In previous studies cited by the authors, researchers found associations between diminished Treg cell function due to downregulation of *FOXP3* and increased asthma severity among children exposed to polycyclic aromatic hydrocarbons, a component of DEP.



*Lead researcher Ho is the Jacob A. Schmidlapp Endowed Chair and professor of the UCMC Department of Environmental Health (DEH). She also serves as the director of the [Center for Environmental Genetics](#) at UCMC. (Photo courtesy of UC)*

The team hypothesized that early and consistent exposure to high levels of traffic pollution would cause transcriptional silencing of *FOXP3* through hypermethylation. They speculated that this downregulation would be predictive of wheezing and asthma in later life, and could be reliably assessed in DNA from saliva.

Subjects in the study were 92 children, selected from the [Cincinnati Childhood Allergy and Air Pollution Study \(CCAAPS\)](#), with a consistent DEP exposure throughout childhood and no exposure to environmental tobacco smoke, which might have been a confounder. This sample was representative of children in the CCAAPS cohort in regard to sex, race, and prevalence of respiratory outcomes.

Participants were classified as nonwheezers or never-wheezers, if there was no parental report in the previous year; transient wheezers, if there was wheezing at ages 1, 2, 3, or 4 but not at age 7, the point at which asthma can be conclusively diagnosed; and persistent wheezers, whose parents reported wheezing at age 7 and during at least one year in ages 1 through 4.

### Increased risk for adverse health effects

Higher levels of *FOXP3* methylation showed significant associations with poor respiratory health outcomes, including:

- Two-fold increase in the mean level of *FOXP3* methylation among persistent wheezers, as compared with nonwheezers.
- Significantly higher mean levels of *FOXP3* methylation among early transient wheezers, than among nonwheezers.
- Three times the risk of persistent wheezing during childhood, for subjects with increased *FOXP3* methylation levels.
- Two times the likelihood of developing asthma for children with increased *FOXP3* methylation.

The study represents the most recent set of findings by NIEHS-funded researchers at UCMC and the [Columbia Center for Children's Environmental Health](#), on biological mechanisms related to the health effects of exposure traffic pollution during windows of susceptibility in fetal and childhood development. Their work has led to the discovery of multiple epigenetic biomarkers of exposure and disease prediction, which may inform innovative public health measures to prevent, reverse, or ameliorate health effects of exposure.

*Citation:* Brunst KJ, Leung YK, Ryan PH, Khurana Hershey GK, Levin L, Ji H, Lemasters GK, Ho SM. 2012. Forkhead box protein 3 (FOXP3) hypermethylation is associated with diesel exhaust exposure and risk for childhood asthma. *J Allergy Clin Immunol*; doi: 10.1016/j.jaci.2012.10.042 [Online 20 December 2012].



*First author Kelly Brunst, Ph.D., who completed her doctoral program last year at UCMC in the division of epidemiology and biostatistics, has worked on several studies ([see story](#)) on environmental exposures and asthma. (Photo courtesy of UC)*



*Senior author Grace LeMasters, Ph.D., is the lead researcher on CCAAPS. (Photo courtesy of Steve McCaw)*

Tang WY, Levin L, Talaska G, Cheung YY, Herbstman J, Tang D, Miller RL, Perera F, Ho SM. 2012. Maternal exposure to polycyclic aromatic hydrocarbons and 5'-CpG methylation of interferon-gamma in cord white blood cells. *Environ Health Perspect* 120(8):1195-1200.

[Return to Table of Contents](#)

## Prenatal inflammation linked to autism risk

By Ed Kang

Maternal inflammation during early pregnancy may be related to an increased risk of autism in children, according to new findings supported by the National Institute of Environmental Health Sciences (NIEHS). Researchers found this in children of mothers with elevated C-reactive protein (CRP), a well-established marker of systemic inflammation.

The risk of autism among children in the [study](#) was increased by 43 percent among mothers with CRP levels in the top 20th percentile, and by 80 percent for maternal CRP in the top 10th percentile. The findings appear in the journal *Molecular Psychiatry* and add to mounting evidence that an overactive immune response can alter the development of the central nervous system in the fetus.

### Fetal origin of brain development

“Elevated CRP is a signal that the body is undergoing a response to an inflammatory insult, for example, a viral or bacterial infection,” said lead scientist [Alan Brown, M.D.](#), professor of clinical psychiatry and epidemiology at Columbia University College of Physicians and Surgeons, New York State Psychiatric Institute, and Mailman School of Public Health. “The higher the level of CRP in the mother, the greater the risk of autism in the child.”

Brown cautioned that the results should be viewed in perspective since the prevalence of inflammation during pregnancy is substantially higher than the prevalence of autism.

“The vast majority of mothers with increased CRP levels will not give birth to children with autism,” Brown said. “We don’t know enough yet to suggest routine testing of pregnant mothers for CRP for this reason alone; however, exercising precautionary measures to prevent infections during pregnancy may be of considerable value.”

“The brain develops throughout pregnancy,” said Linda Birnbaum, Ph.D., director of NIEHS, which funds a broad portfolio of autism and neurodevelopmental-related research. “This has important implications for understanding how the environment and our genes interact to cause autism and other neurodevelopmental disorders.”

The study capitalized on a unique national birth cohort known as the [Finnish Maternity Cohort \(FMC\)](#), which contains an archive of samples collected from pregnant women in Finland, where a component of whole blood referred to as serum is systematically collected during the early part of pregnancy. The FMC consists of



*Along with his FMC research on autism, Brown leads a large birth cohort study on the causes of bipolar disorder in Northern California, as well as a [Conte Center for the Neuroscience of Mental Disorders](#) project on prenatal selective serotonin reuptake inhibitors and neuropsychiatric outcomes in Finland. (Photo courtesy of Alan Brown)*



1.6 million specimens from about 810,000 women, archived in a single, centralized biorepository. Finland also maintains diagnoses of virtually all childhood autism cases from national registries of both hospital admissions and outpatient treatment.

From this large, national sample, the researchers analyzed CRP in archived maternal serum corresponding to 677 childhood autism cases and an equal number of matched controls. According to the team, the findings were not explained by maternal age, paternal age, gender, previous births, socioeconomic status, preterm birth, or birth weight. The work was conducted in collaboration with investigators in Finland, including the University of Turku and the National Institute for Health and Welfare in Oulu and Helsinki.

“Studying autism can be challenging, because symptoms may not be apparent in children until certain brain functions, such as language, come online,” said Cindy Lawler, Ph.D., head of the NIEHS Cellular, Organ, and Systems Pathobiology Branch and program lead for the Institute’s extramural portfolio of autism research. “This study is remarkable, because it uses biomarker data to give us a glimpse back to a critical time in early pregnancy.”

### **A public health message about prevention**

This work is expected to stimulate further research on autism, a complex disease that presents significant challenges to identifying causes. Future studies may help define how infections, other inflammatory insults, and the body’s immune response interact with genes to elevate the risk for autism and other neurodevelopmental disorders. Preventive approaches addressing the environmental causes of autism may also benefit from additional research.

The study was funded primarily by an American Recovery and Reinvestment Act grant from NIEHS, with additional support from the National Institute of Mental Health.

*Citation:* [Brown AS, Sourander A, Hinkka-Yli-Salomäki S, McKeague IW, Sundvall J, Surcel HM. 2013. Elevated maternal C-reactive protein and autism in a national birth cohort. Mol Psychiatry; doi: 10.1038/mp.2012.197 \[online 22 January 2013\].](#)

(Ed Kang is a public affairs specialist in the Office of Communications and Public Liaison, and a regular contributor to the Environmental Factor.)

[Return to Table of Contents](#)

## **Uncovering the genetic component in nicotine addiction**

*By Eddy Ball*

Two new studies in the Jan. 24 issue of the New England Journal of Medicine offered good news about living longer, for people who can quit smoking by early middle age or sooner. But that good news is less meaningful for the approximately 44 percent of daily smokers Washington University School of Medicine in St. Louis psychiatrist Laura Bierut, M.D., estimates are truly nicotine dependent and the most resistant to smoking cessation.

Bierut, a National Institute on Drug Abuse (NIDA) grantee and member of the NIDA Genetics Consortium, was at NIEHS Jan. 23 to report on her work uncovering the genetic component in nicotine addiction, with a talk on “The interplay of environment and genes in smoking behaviors,” hosted by NIEHS Health Science Administrator Kimberly McAllister, Ph.D.

## The progression of nicotine addiction

Bierut opened the prologue to her narrative by discussing a 2005 study on a gene variant related to macular degeneration, which she said marked the beginning of the new generation of large-scale genome-wide association studies (GWAS). “That really just changed our paradigm of genetic studies,” she explained. “Where we are now, is we are really thinking about how these genetic studies are going to move forward with improving human health and the public health of the population.”

Describing the process of becoming a smoker as a multi-step progression, Bierut said that nearly 60 percent of people in a poll conducted in St. Louis and Detroit, who had smoked that first cigarette, ultimately became smokers. “You become a smoker when you smoke 100 cigarettes in your lifetime. Past this threshold of 100 cigarettes, 85 percent become daily smokers.”

Research by Bierut and others contrasted the genetic profiles of what she described as the extremes of the smoker phenotype — at one end, people who can smoke every so often without becoming nicotine-dependent, or chippers, and, at the other end, nicotine addicts. Their findings led to the chromosome 15 region, where key polymorphisms in nicotinic receptor genes show a very specific association with nicotine dependence, lung cancer, chronic obstructive pulmonary disease, and cardiovascular diseases.

“Across the chromosomes, there are hints of other genetic findings, but you have this really screaming hot association in the chromosome 15 region,” she said. “It appears to change the [nicotinic] receptor functionally. ... I call this the Mister Big finding.”

## Translating GWAS into primary prevention and treatment

According to Bierut, there is an interplay of variants in the *CHRNA5* gene and environmental factors, including parental monitoring, peer smoking, and early-onset smoking, that may help scientists and public health advocates more effectively encourage young people to delay the start of smoking, or completely avoid it, and give nicotine-dependent smokers a better chance at success when they try to quit.

“The environment is really the area that we can change,” Bierut said, pointing to the effects of higher taxes on tobacco and other preventive measures. She cited research findings, indicating that early-onset of smoking amplifies genetic risk. “This [further] supports efforts to keep young people from smoking.”



*The take-it-or-leave-it smokers, or chippers, who make up about 20 percent of daily smokers, were important in forming Bierut's thinking about nicotine addiction. “They [smoke occasionally] but do not seem to be transitioning to nicotine dependence. ... This group is the important [extreme] phenotype to study.” (Photo courtesy of Steve McCaw)*



*Bierut's audience included scientists from the NIEHS grants program and in-house research groups, as well as two of her colleagues now at RTI — Senior Research Scientist Eric Johnson, Ph.D., and Genetic Epidemiologist Dana Hancock, Ph.D., who completed her postdoctoral fellowship in the NIEHS Epidemiology Branch. (Photo courtesy of Steve McCaw)*

According to Bierut, studies of participants receiving placebo in smoking cessation groups pointed to another use for the Mister Big finding in the choice of treatment protocols for people who want to quit. The genetic variant that places smokers at the highest risk for nicotine dependence, she explained, is also placing them at highest risk for failed smoking cessation.

Variant status is also predictive of which smokers will benefit the most from pharmacologic treatment. “Depending on your genotype, you are responding very differently to the active pharmacologic treatment for smoking cessation,” Bierut concluded. Patients with the lowest genetic risk can often quit on their own, while those with the high-risk variant should be targeted for pharmacologic intervention to help continue the downward trends of cigarette consumption and deaths from smoking, which still kills some 400,000 people in the U.S. each year.

[Return to Table of Contents](#)

## NIEHS research featured in The Journal of Immunology

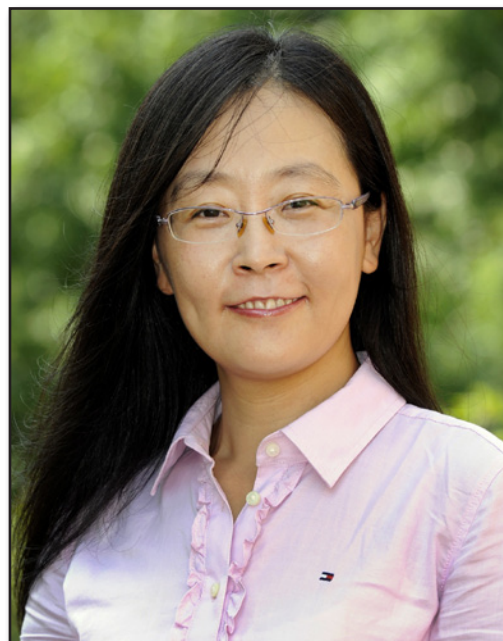
*By Robin Arnette*

When pathogens attack the human body, its immune system mounts an aggressive defense by sending highly specialized cells, called macrophages that recognize, bind, and ingest the infectious agents. One of the proteins involved in this molecular battle is macrophage-1 Ag (Mac-1), a receptor that appears on the surface of many types of immune cells, including macrophages. Previous studies have determined that Mac-1 recognizes a number of molecules associated with pathogen invasion or tissue damage, for example, endotoxin from gram negative bacteria and aggregated proteins, but its role in virus infection was largely unknown.

Now, NIEHS scientists have found that Mac-1 also interacts with double-stranded RNA (dsRNA), the byproduct of a viral infection. After viral dsRNA spills out of a dying immune cell and enters the extracellular space, Mac-1 intercepts it and mediates host immune responses. The Journal of Immunology published the findings Jan. 1 and featured the research in its “In This Issue” section, a highlight of the top 10 percent of articles published in the journal.

Huiming Gao, M.D., Ph.D., is corresponding author on the paper and a research fellow in the NIEHS Neuropharmacology Group, headed by [Jau-Shyong Hong, Ph.D.](#) She said this paper distinguishes itself from other viral studies because it identifies Mac-1 as a novel receptor for dsRNA and uncovers a distinct downstream signaling pathway that is independent of dsRNA’s known receptor, Toll-like receptor 3.

“In the virus field, many scientists study how the virus enters the cell or how it replicates inside the host cell,” Gao said, “but, for our work, we examined how the viral product, released from broken host cells, triggers the host’s fight against the infection.”



*Gao’s medical background makes her well-suited for studying neurodegenerative illnesses. (Photo courtesy of Steve McCaw)*



## Targeting neurodegenerative diseases

The analysis that Hong and his group performed expands scientists' understanding of this important receptor and may lead to discovery of a therapeutic target for viral-induced illnesses. The Neuropharmacology Group focuses on neurodegenerative diseases, and Hong said a growing amount of evidence proposes that viruses, one of many environmental determinants, are important risk factors for chronic neuroinflammatory brain diseases, such as Parkinson's disease.

"If we are able to modulate the degree of inflammation in the brain by targeting the Mac-1 pathway, it may help the survival of neurons," Hong said.

Parkinson's disease isn't the only viral condition that Hong's group has in its crosshairs. [Ross River virus](#), mainly found in Western Australia and several South Pacific islands, is transmitted by mosquitoes and causes joint inflammation and muscle degeneration. Understanding how Mac-1 stimulates the host immune response could lead to relief for this malady, too.

For future studies, paper first author Hui Zhou, Ph.D., and others at NIEHS will use brain macrophage-like immune cells, called microglia, to study how the interaction of viral dsRNA and microglial Mac-1 affects neuronal survival in Parkinson's disease. The work could lead to advances in conditions as varied as Huntington's disease, Alzheimer's disease, and multiple sclerosis.

*Citation:* [Zhou H](#), [Liao J](#), [Aloor J](#), [Nie H](#), [Wilson BC](#), [Fessler MB](#), [Gao HM](#), [Hong JS](#). 2013. CD11b/CD18 (Mac-1) is a novel surface receptor for extracellular double-stranded RNA to mediate cellular inflammatory responses. *J Immunol* 190(1):115-125.

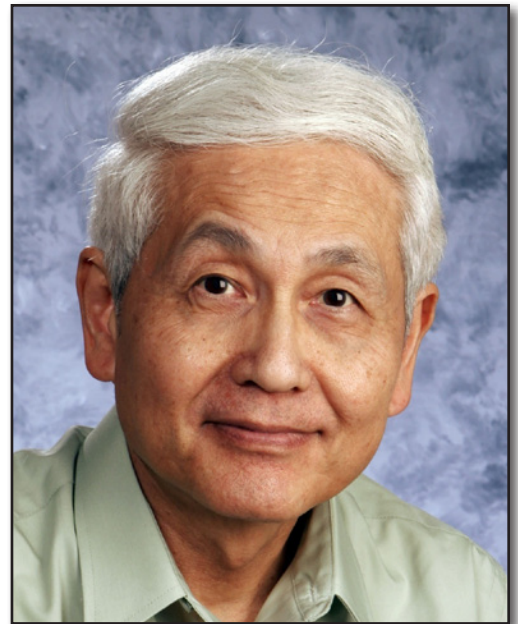
[Return to Table of Contents](#)

## This month in EHP

News features in the February issue of [Environmental Health Perspectives \(EHP\)](#) describe potentially promising developments in environmental health.

### Phage Renaissance: New Hope Against Antibiotic Resistance

Bacteriophages, or phages for short, are natural viral predators that target bacteria, but leave mammalian and plant cells unscathed. Before the widespread use of antibiotics, physicians successfully treated a variety of infections with phages. Today, faced with the growing threat of antibiotic-resistant bacteria, researchers are reinvestigating phages as a potential solution for a variety of medical, agricultural, and environmental problems.



*Hong said that prior to his group's results, most researchers usually thought that Mac-1 only interacted with a variety of bacteria. (Photo courtesy of Steve McCaw)*



<http://twitter.com/ehponline>

## Sunset for Leaded Aviation Gasoline?

Leaded aviation gasoline, or avgas, is one of the few fuels in the United States to still contain lead, and it's the single largest source of lead emissions in the country, according to the U.S. Environmental Protection Agency (EPA). An appropriate replacement fuel has remained surprisingly elusive and, meanwhile, EPA has been conducting studies to clarify how airport lead emissions affect National Ambient Air Quality Standards compliance. The search for a replacement fuel got a boost in 2012, when a committee of the Federal Aviation Administration issued recommendations and criteria for identifying and approving an unleaded avgas, and the agency opened a new office charged with overseeing the certification of a new fuel.

## Podcast: Air Pollution and Birth Outcomes, With Tracey Woodruff

NIEHS grantee [Tracey Woodruff, Ph.D.](#), discusses her forthcoming research on air pollution and birth outcomes, which involved 14 study groups on five different continents. She describes not only the new results, but also the logistical challenges involved in coordinating such a large study and standardizing data across study groups, in a [podcast](#) to be posted Feb. 6, along with the embargoed research paper.

Featured commentaries, reviews, and research this month include:

- *In Utero* and Childhood Polybrominated Diphenyl Ether (PBDE) Exposures and Neurodevelopment in the CHAMACOS Study
- Urinary Biomarkers for Phthalates Associated with Asthma in Norwegian Children
- Long-term Exposure to Road Traffic Noise and Incident Diabetes: A Cohort Study
- Toxicological Function of Adipose Tissue: Focus on Persistent Organic Pollutants

[Return to Table of Contents](#)

## Extramural papers of the month

*By Nancy Lamontagne*

- Black carbon from kerosene lamps contributes to climate change
- Bioanalytical tool measures toxicity of bioavailable complex mixtures
- Developing new chemicals free of endocrine disruptors
- Mechanism for increased Parkinson's disease risk from benomyl exposure



Read the current Superfund Research Program [Research Brief](#). New issues are published on the first Wednesday of each month.

## Black carbon from kerosene lamps contributes to climate change

A study, funded in part by NIEHS, shows that the kerosene-fueled wick lamps, commonly used in developing-country households, are a significant source of black carbon emissions. Replacing these lamps with cleaner light sources would benefit people's health and the planet.

Black carbon contributes to global warming, because it absorbs light and heats the atmosphere. The researchers conducted both field and laboratory testing of kerosene wick lamps, finding that 7 to 9 percent of the kerosene consumed is converted to carbonaceous particulate matter that is nearly pure black carbon. From these emission factors, they estimated that kerosene lighting emits 270,000 metric tons of black carbon per year, a 20-fold increase from previous estimates.

Radiative forcing is a common measure of climate impact that describes the change in Earth's net energy balance brought on by a constituent(s) at the top of the atmosphere. The researchers estimated the aerosol climate forcing on atmosphere and snow from kerosene wick lamps is 7 percent of black carbon forcing from all other energy-related sources.

*Citation:* [Lam NL, Chen Y, Weyant C, Venkataraman C, Sadavarte P, Johnson MA, Smith KR, Brem BT, Arineitwe J, Ellis JE, Bond TC. 2012. Household light makes global heat: high black carbon emissions from kerosene wick lamps. Environ Sci Technol 46\(24\):13531-13538. \[Story\]\(#\)](#)

[Return to Table of Contents](#)

## Bioanalytical tool measures toxicity of bioavailable complex mixtures

NIEHS grantees report that a bioanalytical tool, known as Biological Response Indicator Devices Gauging Environmental Stressors (BRIDGES), can detect highly resolved spatial and temporal differences in bioavailable chemicals in the environment, and measure the toxicity of these environmental mixtures.

BRIDGES combines passive sampling and an embryonic zebrafish developmental toxicity bioassay to measure the toxicity of bioavailable complex mixtures. To test the approach, the researchers used passive sampling devices to sequester and concentrate bioavailable organic contaminants in the Willamette and Columbia Rivers within and outside of the Portland Harbor Superfund site in Portland, Ore.

They analyzed extracts from the devices to check for the presence of polycyclic aromatic hydrocarbon (PAH) compounds and 1,201 chemicals of concern using deconvolution-reporting software. The researchers then examined the developmental toxicity of the extracts with the embryonic zebrafish bioassay. Using multivariate modeling, they linked chemicals with toxic effects and identified the PAH analytes most highly correlated with observed toxicity. The researchers say that the BRIDGES tool could be useful for a wide range of environmental monitoring projects.

*Citation:* [Allan SE, Smith BW, Tanguay RL, Anderson KA. 2012. Bridging environmental mixtures and toxic effects. Environ Toxicol Chem 31\(12\):2877-2887.](#)

[Return to Table of Contents](#)



## Developing new chemicals free of endocrine disruptors

NIEHS grantees and scientists are part of a group of researchers proposing a new Tiered Protocol for Endocrine Disruption (TiPED) for detecting chemicals with possible endocrine disrupting properties. The voluntary protocol could help manufacturers and chemists avoid introducing endocrine disrupting chemicals during product and chemical development.

Endocrine disruptors are found in many consumer products and can lead to developmental, reproductive, neurological, and immune problems. TiPED's five testing tiers range from broad evaluation based on computer modeling, to specific assays based on cells and whole organisms. The tiers progress in complexity and cost, as well as the reliability of results. A user can use all the tiers or start with any tier in the system.

In a proof-of-principle test, the researchers used TiPED to analyze six endocrine disrupting chemicals, each with different endocrinological mechanisms. Each chemical was identified as endocrine active by one or more tiers. The scientists also established a plan to incorporate new assays into the protocol, as scientific understanding of endocrine disruption continues to advance.

*Citation:* Schug TT, Abagyan R, Blumberg B, Collins TJ, Crews D, DeFur PL, Dickerson SM, Edwards TM, Gore AC, Guillette LJ, Hayes T, Heindel JJ, Moores A, Patisaul HB, Tal TL, Thayer KA, Vandenberg LN, Warner JC, Watson CS, vom Saal FS, Zoeller RT, O'Brien KP, Myers JP. 2013. Designing endocrine disruption out of the next generation of chemicals. *Green Chem* 15(1):181-198.

[Return to Table of Contents](#)

## Mechanism for increased Parkinson's disease risk from benomyl exposure

NIEHS grantees integrated findings from cell, animal, and population studies to reveal how exposure to the fungicide benomyl increases risk for Parkinson's disease. Their work suggests that the neurodegenerative process by which benomyl acts might also occur in people with Parkinson's disease who were not exposed to benomyl.

Benomyl was discontinued in the U.S. in 2001, but is still used in some countries. The researchers' population studies indicated an association between higher exposure to benomyl and increased Parkinson's disease risk. They tested the effects of benomyl on cell cultures, finding that the fungicide inhibited aldehyde dehydrogenase (ALDH) activity and altered dopamine levels. Cell culture experiments and tests using a zebrafish model of Parkinson's disease showed that benomyl brought on selective loss of dopamine-producing neurons while not affecting other types of neurons. The cell loss decreased when the researchers added an enzyme that reduced the formation of 3,4-dihydroxyphenylacetaldehyde (DOPAL), a reactive dopamine metabolite.

These results, together with those from previous studies, provide evidence for a Parkinson's disease pathway in which benomyl inhibits ALDH, leading to DOPAL accumulation and degeneration of dopamine-producing neurons. This ALDH pathway may explain why dopamine-producing neurons are selectively vulnerable in Parkinson's disease and could also provide a new target for therapeutic drugs.

*Citation:* Fitzmaurice AG, Rhodes SL, Lulla A, Murphy NP, Lam HA, O'Donnell KC, Barnhill L, Casida JE, Cockburn M, Sagasti A, Stahl MC, Maidment NT, Ritz B, Bronstein JM. 2012. Aldehyde dehydrogenase inhibition as a pathogenic mechanism in Parkinson disease. *Proc Natl Acad Sci U S A* 110(2):636-641. [Story](#)

(Nancy Lamontagne is a science writer with MDB Inc., a contractor for the NIEHS Division of Extramural Research and Training, Superfund Research Program, and Worker Education and Training Program.)

[Return to Table of Contents](#)

## Intramural papers of the month

*By Monica Frazier, Ashley Godfrey, Sonika Patial, and Bhargavi Rao*

- Interdependence of estrogen receptor alpha domains in maintaining male fertility
- Mismatch repair balances leading and lagging strand DNA replication fidelity
- Novel role of Galpha(i) subfamily of G-proteins in axial skeleton development
- The involvement of leptin in fatty liver disease

### Interdependence of estrogen receptor alpha domains in maintaining male fertility

In a new study, NIEHS scientists determined that the C-terminal transcriptional activation function domain (AF-2) of estrogen receptor alpha (ERalpha) regulates the activity of a separate N-terminal AF-1 region. AF-2 occurs on helix 12 of the ligand-binding domain of ERalpha and is crucial for maintaining male reproductive tract function. The work will help scientists understand which genes ERalpha regulates in males, both directly and indirectly.

Although the hormone estrogen and one of the receptors it activates, ERalpha, are usually associated with females, they also play an important role in male reproduction. Several cell types in the male reproductive system express ERalpha, and its absence results in infertility in male mice.

Using mouse models, the researchers showed that a mutation in ERalpha's AF-2 results in male infertility because the seminiferous tubules, or the structures that produce sperm, are abnormally shaped and the efferent ducts, which connect the testis to the epididymis, display altered gene expression. They also demonstrated that activating this AF-2 mutant receptor with a receptor agonist, tamoxifen, restores fertility.

The data suggested that N-terminal AF-1 is unable to independently regulate the expression of key genes involved in reproductive tract function. AF-2 is required for proper function of AF-1, specifically, and ERalpha, overall. **(BR)**

*Citation:* [Arao Y, Hamilton KJ, Goulding EH, Janardhan KS, Eddy EM, Korach KS](#). 2012. Transactivating function (AF) 2-mediated AF-1 activity of estrogen receptor alpha is crucial to maintain male reproductive tract function. *Proc Natl Acad Sci U S A* 109(51):21140-21145.

[Return to Table of Contents](#)

# Mismatch repair balances leading and lagging strand DNA replication fidelity

Researchers in the NIEHS Laboratory of Molecular Genetics report new findings on the balancing act DNA mismatch repair plays between the two replicating DNA strands and the three replication polymerases in yeast.

The authors used strand specific DNA probes to confirm the hypothesis that DNA polymerases alpha, delta, and epsilon frequently incorporate ribonucleotides into the yeast genome in a strand-specific manner during DNA replication. The results reinforce previous conclusions made by the group, headed by Thomas Kunkel, Ph.D., that Pols delta and alpha are primarily responsible for lagging strand synthesis, while Pol epsilon synthesizes the leading strand.

The authors found that mismatch repair efficiency correlates first with the potential phenotypic severity of a mutation and then with the rate of mismatch generation, an advantageous evolutionary strategy for focusing repair where it is most needed. For instance, single-base insertions and deletions (indels) can have more severe phenotypic potential than base-base mismatches, on average. Therefore, indels are more efficiently repaired than base-base mismatches. Among base-base mismatches, which have roughly equal phenotypic potential, the more common class known as transitions are more efficiently repaired than the less common transversion class. Likewise, between the three polymerases, mismatch generation and repair are generally complementary.

The authors also came upon a natural DNA sequence that completely prevents the repair of an adjacent mismatch, even though mismatches of the same type are efficiently repaired in other sequence contexts. **(MF)**

*Citation:* [Lujan SA](#), [Williams JS](#), [Pursell ZF](#), [Abdulovic-Cui AA](#), [Clark AB](#), [Nick-McElhinny SA](#), [Kunkel TA](#). 2012. Mismatch repair balances leading and lagging strand DNA replication fidelity. *PLoS Genet* 8(10):e1003016.

[Return to Table of Contents](#)

# Novel role of Galpha(i) subfamily of G-proteins in axial skeleton development

In a new study, NIEHS Laboratory of Neurobiology scientists offer a novel role for the Galpha(i) subfamily of G proteins in axial skeleton development.

The heterotrimeric G protein alpha subunits are cytoplasmic proteins that play a role in coupling several types of cell surface receptors to intracellular effector molecules, such as ion channels and enzymes. Researchers utilized a knockout mouse approach to create a targeted loss of function mutation in *Gnai3*, one of three genes that encode the inhibitory class of alpha subunits, Galpha(i).

The loss of function mutation resulted in mice with fused ribs and lumbar vertebrae, suggesting that Galpha(i) is required in somite derivatives during development, and severity of the abnormalities was increased when the other genes encoding Galpha(i) were mutated in addition to *Gnai3*. Moreover, this phenotype was specific to the inbred mice generated on a 129/SvEv background and was altered in mice with a mixed C57BL/6 X 129/SvEv background.



The results of this study shed light on a previously unknown role for G protein-coupled signaling pathways in the development of the axial skeleton. In addition, the study demonstrates the effects of genetic background on phenotype. **(SP)**

*Citation:* [Plummer NW, Spicher K, Malphurs J, Akiyama H, Abramowitz J, Nurnberg B, Birnbaumer L.](#) 2012. Development of the mammalian axial skeleton requires signaling through the Galpha(i) subfamily of heterotrimeric G proteins. *Proc Natl Acad Sci U S A* 109(52):21366-21371.

[Return to Table of Contents](#)

## The involvement of leptin in fatty liver disease

Investigators at NIEHS, NTP, Duke University, and the University of South Carolina recently found that protein radical formation, mediated by leptin, is caused by peroxynitrite formation, a type of oxidative stress mechanism. This process intensifies inflammatory liver lesions, called steatohepatitic lesions, in mice subjected to diet-induced obesity. When the mice were given carbon tetrachloride, a model hepatotoxin, their circulatory leptin levels increased over and above the levels found in obesity. This study furthers understanding of the steps involved in environment-linked non-alcoholic steatohepatitis, and suggests that an increase in liver leptin levels causes oxidative stress and augments progression of steatohepatitis.

Steatohepatitis, a consequence of fatty liver disease, is characterized by inflammation of the liver during steatosis, or fat accumulation. Both obesity and oxidative stress are believed to cause non-alcoholic steatohepatitis, and progression from steatosis to full steatohepatitic lesions is believed to require a second catalyst. Since these lesions are commonly associated with oxidative stress, attributed to high levels of leptin and other mediators, the investigators used obese mice to analyze the role of leptin in inducing oxidative stress and activating macrophages following carbon tetrachloride exposure.

Investigators concluded that leptin-induced formation of peroxynitrite was important for the resulting inflammatory process and progression of the disease. **(AG)**

*Citation:* [Chatterjee S, Ganini D, Tokar EJ, Kumar A, Das S, Corbett J, Kadiiska MB, Waalkes MP, Diehl AM, Mason RP.](#) 2012. Leptin is key to peroxynitrite-mediated oxidative stress and Kupffer cell activation in experimental non-alcoholic steatohepatitis. *J Hepatol*; doi:10.1016/j.jhep.2012.11.035 [Online 01 December 2012].

(Monica Frazier, Ph.D., is an Intramural Research Training Award (IRTA) fellow in the NIEHS Laboratory of Molecular Genetics. Ashley Godfrey, Ph.D., is an IRTA fellow in the NIEHS Laboratory of Molecular Carcinogenesis. Sonika Patial, D.V.M., Ph.D., is a visiting fellow in the NIEHS Laboratory of Signal Transduction. Bhargavi Rao, Ph.D., is an IRTA fellow in the NIEHS Laboratory of Neurobiology.)

[Return to Table of Contents](#)

# Inside the Institute

## NIEHS surpasses 2012 CFC goal

*By Bailey Schug*

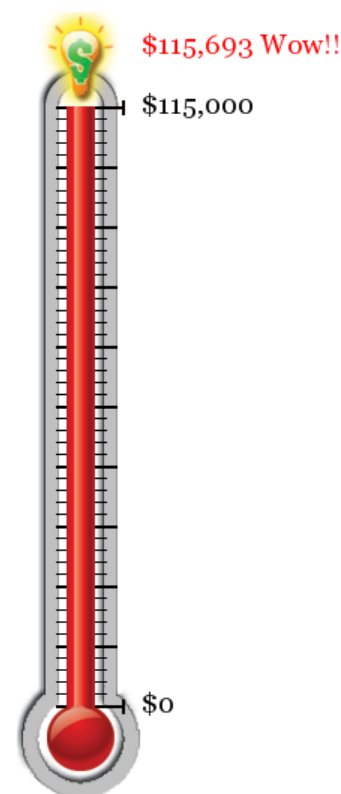
It was another record-setting year for NIEHS participation in the Combined Federal Campaign (CFC), with pledges exceeding the 2012 goal of \$115,000. After the institute kicked off the campaign in September, employees set to work raising funds for nonprofits in the community and around the world that make a difference in the lives of people and animals in need of help. The CFC is the largest workplace giving campaign in the world, and the employees who give through it are among the most generous.

The 2012 CFC at NIEHS not only reached its goal, but exceeded it with total donations of \$115,693.41. Co-chairs Claire Long and Scott Redman, along with many hardworking and dedicated volunteers, spent the last three months of 2012 hosting a full schedule of events, making sure this year's campaign would be one for the books. The CFC co-chairs credit the hard work of key workers for making the 2012 campaign successful.

"While the final CFC total of \$115,693.41 is impressive and exciting," Long said, "reaching that achievement lies completely at the hands of the incredibly generous and inspiring NIEHS employees." NIEHS/NTP Director Linda Birnbaum, Ph.D., was supportive and encouraging throughout the campaign, as well as a participant in many of the campaign's special events.

"NIEHS employees rose to the incredible challenge, and gave with compassion and generosity at unprecedented levels," Long said. "We are just honored to have been a part of the campaign and experience first-hand the generosity of NIEHS employees."

(Bailey Schug studies health promotion at Appalachian State University. She is an intern with the NIEHS Office of Communications and Public Liaison.)



*NIEHS surpassed its goal of \$115,000, setting yet another record, by raising \$115,693 from more than 200 pledges and donations.*



*Long is a member of NIEHS Associate Director for Management Joellen Austin's staff. (Photo courtesy of Steve McCaw)*



*Redman is a member of the NIEHS Financial Management Branch. (Photo courtesy of Steve McCaw)*

[Return to Table of Contents](#)

# NIEHS biologist honored for award-winning photography

*By Ian Thomas*

John Petranka has spent his career studying the environment through the lens of a microscope, most notably as a biologist with the NIEHS [Calcium Regulation Group](#). In his spare time, however, Petranka still enjoys viewing the world around him — albeit through a lens of a slightly different kind.

A thriving amateur photographer, Petranka is being honored by *Wildlife in North Carolina* magazine as one of this year's winners in the publication's eighth annual [wildlife photography competition](#), with first prizes in the categories of invertebrates and wild plants, as well as a bird photo featured on the inside back cover.

"I'm absolutely delighted about this award, though admittedly a bit humbled," said Petranka, a longtime resident of Chapel Hill who took up the hobby just four years ago. "This contest attracts some extraordinary work from some really talented people, many of whom are a lot more experienced at this than I am."

## A natural eye for the craft

A native of Alabama and a graduate of Auburn University's zoology program, Petranka moved to the Triangle in 1984, where he says the opportunities for picture taking are as rich as the landscape itself.

"The zoning restrictions in our area of Orange County have done a nice job preserving the rural habitat for native plants and animals — a real treat for photographers," said Petranka, an avid fan of the region's spring wildflower season.

Fellow photographer and colleague Steve McCaw added, "John's macro-photography work is some of the best I've ever seen, and as anyone who's ever attempted that kind of shoot will tell you, it's an incredibly challenging technique to master."

## The beauty of science

Currently engaged in a study of calcium signaling in cells, Petranka manages the lab in which he works, as well as his group's transgenic mouse colony. Still, whether he's conducting fluorescence-based studies with his labmates or shooting moss in his back yard, Petranka freely admits that both serve a key purpose.

"For me, science and photography each represent a unique way to learn about the living world around us," said Petranka. "In the lab, I get to study the remarkable intricacies of things like cellular function to help improve human health, whereas, with photography, I still examine many of those same beautiful complexities, but from a more aesthetically pleasing point of view."



*NIEHS biologist and award-winning nature photographer John Petranka (Photo courtesy of Steve McCaw)*

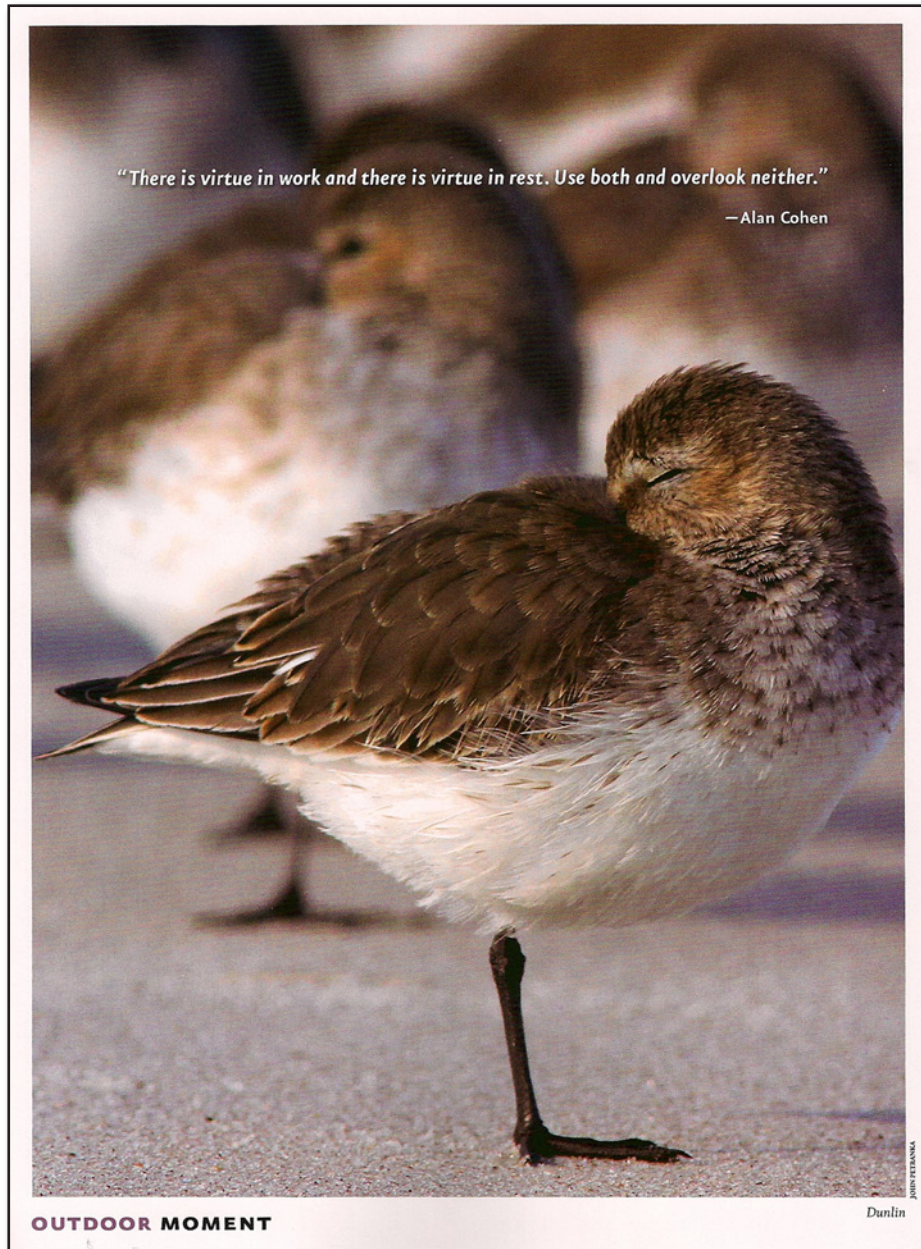


*By encouraging public participation in nature photography, Wildlife in North Carolina magazine seeks to foster a greater understanding and appreciation of the state's indigenous wildlife and natural places. The cover features a close up of a striped horsefly by grand winner Mickey Moten. (Photo courtesy Wildlife in North Carolina magazine)*



The January/February issue of Wildlife in North Carolina, featuring the 2012 winners of the wildlife photo competition, is available online via the North Carolina Wildlife Resources Commission [website](#), or on newsstands around the North Carolina Triangle region.

(Ian Thomas is a public affairs specialist with the NIEHS Office of Communications and Public Liaison and a regular contributor to the Environmental Factor.)



*Petranka's bird at rest graced the inside back cover of the issue. (Photo courtesy of John Petranka)*



*Petranka's praying mantis was taken at the Triangle Land Conservancy's Johnston Mill Nature Preserve. (Photo courtesy John Petranka)*



*Petranka notes that both of his award-winning photos, including dewy grass, above, were taken within a half-mile of his home in Orange County. (Photo courtesy of John Petranka)*

[Return to Table of Contents](#)



# Neighbors in the house

By John Schelp

A group of 22 high school chemistry students from nearby [Kestrel Heights School \(KHS\)](#) visited NIEHS Jan. 23 for a tour of the facility, much like hundreds of students each year who come to the campus in Research Triangle Park, N.C. The tour was organized by the NIEHS [Office of Science Education and Diversity](#).

One thing in particular set this group apart, however. In the mid-1980s, their science teacher, Andrew Joseph, Ph.D., was a postdoctoral fellow in the Molecular Biophysics Group on the old north campus headed by lead researcher Bob London, Ph.D. Joseph discovered his passion in teaching high school students and decided to follow one of the roads less taken by NIH postdocs.

KHS Executive Director Tim Dugan also joined the group as they went on a walking tour of the Rall Building; learned about the NIH Summer Internship Program from Debbie Wilson; listened to postdoctoral fellow Danielle Watts, Ph.D., talk about her career; and enjoyed science talks by London and staff scientist Geoff Mueller, Ph.D., in the NIEHS Nuclear Magnetic Resonance (NMR) Center.

(John Schelp is a special assistant for community engagement and outreach in the NIEHS Office of Science Education and Diversity.)

[Return to Table of Contents](#)



KHS students joined Joseph, center in brown suit, and Dugan, right, for the tour of NIEHS. (Photo courtesy of John Schelp)



Mueller explained the operation of the NMR as the KHS students looked on. (Photo courtesy of John Schelp)



National Institute of  
Environmental Health Sciences

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